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TRACHOMA IN THE AMERICAN NEGRO RACE.

By J. Bordley, M. D.

The title of this paper rather implies a belief on my part that the American negro race is subject to, probably the most dreaded of all eye diseases, trachoma. Indeed this paper was written with the idea in mind that such a thing is a mere theory impossible of proof by any existing data. After a careful review of the literature I am not convinced that any case has been recorded of trachoma in the American negro. Indeed not one true bill was found.

Dr. Swan Burnett had the distinction of first calling the attention of the profession to this interesting condition in 1876. Theobald, Hamilton, and many other distinguished oculists have written articles substantiating his views. These men have all enjoyed large experience in the treatment of negroes and the weight of their evidence is very convincing.

In reporting cases of trachoma in the black race unfortunately the essential characteristics of the disease have in the majority of instances been overlooked. It seems totally unnecessary to a few writers that the cases should bear some resemblance, either etiologically, symptomatically, or as regards the sequelæ, to the disease as it occurs in the white race. In determining what trachoma is are we to consider macroscopical signs only? Have we the right to class as trachoma cases which do not originate from contagion, do not follow typical courses and terminate without leaving the signs never absent as a result of trachoma in the white race? I am convinced that many cases are reported as the result of that process of elimination recommended by Peter Shaw, in 1738, when he said, in speaking of treating "Simple Ophthalmia": "Let this be continued according to the indication, and if it happen to be without success call it ophthalmia strumosa and treat it as a strumous case."

Trachoma is an acute contagious disease of the conjunctiva, characterized by the formation of papillary overgrowths or granules, or both, and terminating in the formation of cicatricial bands in the conjunctiva of the lids. One of the striking incidents of the disease is an infection of the cornea as a result of minute abrasions caused by constant friction of the diseased lids over the cornea, this infection is called pannus.

The disease was first given serious attention during the Napoleonic wars; since then the morbid processes of this dread affection have been given more attention than any other single ailment of the eye. From Vescht (1807) to Parsons (1905) the most able workers in ophthalmology have been bending every energy to find the cause of and the cure for trachoma. While the cause is not known beyond the fact that the disease is contagious, Hirshberg and Krause described bacilli in acute but failed to find them in chronic cases; Koch believed the Koch-Weeks bacillus to be a concomitant cause with the gonococcus; Sattler described a small diplococcus as did Michel, Schmidt, Raehlmann, Staderini, and others. The micros-

porum furfur, mixed infections, and plasmodia (of which 62 evolution forms have been described) have each and all at some time occupied the attention of the profession and, by some been regarded as the cause of trachoma. There seems to be but one point in the course of the disease which has been definitely settled and upon which all authorities agree, that is, the existence in the conjunctiva of granules is pathognomonic. The essential feature of all clinical trachoma, whether papillar, granular, or mixed is the trachoma follicle. We often find in the human conjunctiva poorly developed follicles and by such authors as Krause and Baumgarten they are regarded as physiological, Waldeyer and Wolfring, however, take the opposite view, regarding them always as pathological.

While we must undoubtedly agree that granules are never seen in the conjunctiva except as a symptom of trachoma we must not at the same time lose sight of the fact that many of our leading text-books in describing the disease have confused follicles with granules. I have no doubt from the description of some of the reported cases in the negro that the surgeon was dealing with a rather typical case of follicular conjunctivitis and, following the lead of some text-book had confused follicles with granules. While we agree that follicles are necessary to trachoma we consider them in no sense pathognomonic. Even in describing follicles we must bear in mind that other conditions can so closely simulate this condition as to require a microscopical examination to determine the difference. The follicles which are found in trachoma are definite anatomical structures, consisting of "reticular tissue of the adenoid layer of the conjunctiva, lymphoid elements in the meshes of the stroma, vessels which surround and send sparse capillaries into the follicle, and a fibrous tissue capsule." We must follow these follicles from the time they make their appearance to the time of their disappearance. In follicular conjunctivitis they decrease in size as the patient improves, ultimately either disappearing entirely leaving no sequelæ or, as is more common, returning from time to time to start fresh trouble; in trachoma resorption of these follicles may take place at any stage, by mere retrogression without softening, or, as is more usually the case, by degenerative changes which take place in the cells, dependent according to Raehlmann, upon sclerosis of the blood-vessels at the periphery and in the neighboring conjunctiva. No matter which way the disappearance of the follicles is brought about, the space is occupied ultimately by connective tissue. The contraction of this connective tissue always leaves as a permanent mark of former trouble, linear scars.

While I do not say that all the reported cases of trachoma in the American negro are errors in diagnosis still all lack some vital point which I cannot pass over unquestioningly.

It is claimed by Van Milligan that in Turkey the negro is beset by this disease. Fernandez, after an exhaustive study of the subject in Cuba, makes the statement that there the negro enjoys an almost complete immunity. How the American negro gains this immunity is a question yet unsolved. Perhaps, as has been suggested, we should bear in mind the negroes of Turkey may have originally belonged to entirely different tribes, may have been reared under vastly different circumstances from the negroes in America. The possibilities from the introduction of a different strain must not be overlooked. If the American negroes are not immune to this disease they certainly possess the power of keeping it to themselves and the happy faculty of getting well and leaving no trace of the disease in either cornea or lids.

I wish here to report three cases which several of my colleagues as well as myself diagnosticated trachoma. The first was a man, aged 31. He is a typical negro, black, ignorant, and stupid. On applying for treatment he said his right eye—the only one affected—had been "bad" for two weeks, pained him very much and "the lids stuck together every morning." I found the lids swollen and tense, a sero-mucus discharge constantly dripping from between the closed lids, the ocular conjunctiva was œdematous and injected, photophobia was intense, iris clear and pupil normal, cornea clear. On everting the upper lid, which was accomplished with the greatest difficulty, I discovered in the retrotarsal folds and in the conjunctiva of the tarsus many small, nodular masses. These masses were so situated as to be definitely outlined and the epithelium so pushed ahead of them as to form small mound-like projections. The conjunctiva over the upper tarsal cartilage had enlarged papillæ giving the conjunctiva the appearance of soft fine velvet. A most diligent search, which was often repeated, failed to demonstrate any grey, translucent, hemispherical bodies which are pathognomonic of granular trachoma.

A culture taken from the cul-de-sac of the conjunctiva developed the xerosis bacillus; this organism was also cultivated from one of the nodular masses. A section from one of the nodular masses showed only a dense round-cell infiltration of the tissues, there was no attempt at encapsulation and no definite reticular or blood-vessel formation could be described, while the epithelium was more flattened than normal the change was insignificant. Attempts at animal inoculations with a pure culture of the organism were negative.

A 20 per cent solution of protargol was instilled in the eye three times a day as was also a 1 per cent solution of atropine. At the end of two weeks the patient had grown much worse, showing what were considered most definite symptoms of a bad case of trachoma. The trouble was at this time complicated by the formation of three small corneal ulcers. It is not the usual rule to find corneal ulcers in the first stages of trachoma, they most often make their appearance as secondary results in the pannus formation. Up to this time our treatment was without avail, suddenly, however, during the

seventh week the eye began to improve and at the expiration of nine weeks the patient was discharged, cured.

Case No. 2 was also a negro man, about 31. He was rather more intelligent than the one to whom I have just referred. His right eye "had been sore" for forty-eight hours before applying for treatment, the lids of the affected eye were so swollen and tense that I could not evert the upper lid or see the retrotarsal fold in the lower lid, the eye was injected and the bulbar conjunctiva very œdematous, cornea and iris clear, and pupil normal. There was a profuse sero-mucus discharge, great pain, and photophobia. I strongly suspected at the beginning a gonococcus infection of the conjunctiva, although the history was absolutely negative and no gonococci were found microscopically.

The case was put on active treatment and placed in the hospital. The treatment consisted of ice-pads, a 40 per cent solution of protargol, and cleansing of the lids as often as was found necessary. The eye responded beautifully to treatment and in a week's time it was possible to evert the lids. In the retro-tarsal folds of the upper lid and over a portion of the tarsal conjunctiva I found the mucus membrane studded with small mound-like projections and the tarsal conjunctiva covered with a velvety papillary structure. A culture taken from the secretion in the retro-tarsal fold developed a pure culture of the Xerosis bacillus. A slide taken from the same secretion showed short, thick bacilli. I regret to say the patient would not allow me to remove any of the conjunctiva, consequently I was unable to study what I believed to be follicular enlargements. Animal inoculations with a pure culture of the organisms were negative.

Two small corneal ulcers made their appearance during the fourth week of the disease. These ulcers disappeared as the lid conditions cleared up. The patient was discharged, cured, nine weeks after the first symptoms had made their appearance.

Case No. 3 differed from the two preceding cases in only two ways: first, both eyes were infected; second, three small tarsal cysts developed in a short time after the case had been discharged. A culture taken from the secretion, developed xerosis bacilli. Sections from nodules showed only the signs of a non-purulent inflammation of the conjunctiva. A slide taken from the contents of one of the chalazia, which were subsequently opened, showed no bacteria. The nodular masses in the conjunctiva, the papillary enlargements in the tarsal conjunctiva, and all the acute symptoms were present in this case as in the others.

I believe no man could have drawn any other conclusion from watching the first symptoms of these three cases than that they were trachoma. Still, now that the cases are well and we sum up the evidence to complete our diagnosis, we must grant that our original observations were based on false premises.

To sum up we found these symptoms which were identical with those of trachoma: a sudden onset, swelling of the lids, a sero-mucus discharge, œdema of the bulbar conjunctiva, apparent follicular enlargements in the palpebral, and papillary overgrowths on the tarsal conjunctiva, pain and photophobia, and the obstinacy of the disease in spite of active antiseptic treatment. Several features necessary to complete a diagnosis of trachoma were, however, absent: no hemispherical, granular bodies were to be discovered in the retro-tarsal folds; the cases did ultimately get entirely well, leaving no scar tissue as a result of the conjunctival trouble; at no time, either during or subsequent to the disease, did a pannus make its appearance; in two cases one eye also was infected; two of the patients were in institutions and frequently, in spite of my advice to the contrary, used towels in common with other people, still, so far as I can find out, no one was infected. I think if we add to these facts the additional evidence that the xerosis bacillus was developed in pure culture in every case and that a histological examination of the supposed follicles in two cases showed only the signs of an acute, non-purulent infection of the conjunctiva with no definite body arrangement such as is found always in trachoma, we can conclude that we were not dealing with trachoma.

Not taking into consideration the bacteriological and pathological findings in these cases does not the evidence seem to indicate that we were not dealing with trachoma? Parsons says that follicles always go on to cicatrization and that trachoma can not exist without the formation in the adenoid layer of the conjunctiva of follicles. Burnett says the only positive evidence of trachoma is the formation of scar tissue in the conjunctiva; Rachlmann coincides with this view and so do all the other authorities on trachoma. These cases of mine show no evidence of scar tissue and never did. Trachoma in the white race is violently epidemic; still two of these cases I report lived in institutions where people were crowded together, and used in common with many others roller towels and yet not another case developed. Trachoma nearly always attacks both eyes: two out of three of my cases had trouble with only one eye. Pannus is nearly always a sequel or an accompaniment of trachoma; then why was it, if my cases were trachoma, not one of them showed the slightest sign of corneal trouble beyond the small ulcers and the scars resulting from them.

I must conclude that under certain circumstances the xerosis bacillus attacks the conjunctiva of the negro and provokes an inflammation which so closely simulates trachoma as to make it impossible in the first stages to make a certain diagnosis. There is this essential difference, however, the inflammation resulting from the xerosis infection gets well and leaves behind it no traces of the active conjunctival trouble. I can readily imagine this difference not holding good if a secondary infection of the conjunctival nodules by a pyogenic organism should take place, for surely then the sloughing ulcers would result in the formation of cicatrices.

The only evidence adduced to prove the disease is caused by the xerosis bacillus is the fact that cultures taken from the secretions and the nodular masses developed the bacillus in pure culture. Animal inoculations were negative.

I wish to thank Dr. J. M. Love for the valuable assistance rendered me in working out the bacteriology of this disease.

A REPORT OF FOUR CASES OF MEMBRANOUS DYSMENORRHEA.

By Elizabeth Morse, M. D.

The term "membranous dysmenorrhea" is applied to cases in which considerable portions of the endometrium are thrown off repeatedly at the menstrual period, usually with pains simulating those of labor. The cases vary in severity from the typical form in which a complete cast of the uterine cavity is discharged at each period with great pain, to the milder ones in which small fragments of the endometrium are passed with only slight symptoms at intervals of several months. Painless cases have occasionally been reported. The passage of a single membrane from the uterus does not constitute a case of membranous dysmenorrhea.

The affection is not a disease *sui generis;* but a condition which develops under varying circumstances, complicates different pathological processes, and presents a variety of microscopic appearances. Some writers have, therefore, suggested that the purely clinical term "membranous dysmenorrhea" be abandoned, and "exfoliative endometritis" (Wyder) (9), or "exfoliation of the menstrual mucosa" (Löhlein) (17) be substituted.

The etiology and pathogenesis of the condition are obscure, and the treatment has been attended with little success. This is due partly to the fact that the affection is in reality rare, and the specimens available for study still more infrequent. The milder cases are often not brought to the physician's attention, while, on the other hand, the diagnosis is frequently made on insufficient clinical data, and without a microscopic examination of the membrane. The latter point is illustrated by the fact that, of eleven specimens sent to the gynecological laboratory of the Johns Hopkins Hospital with the diagnosis of "membranous dysmenorrhea," only three proved, after investigation of the patients' history and examination of the membrane, to be genuine cases. The other specimens showed decidua in four instances, vaginal epithelium in two, and one example respectively of uterine polyp and blood-clot.

The disease was first recognized by Morgagni (1), who reported a case and gave an excellent description of its clinical course. Denman in 1791, also described membranes, but thought them identical with decidual casts, previously described by Hunter. The first microscopic study of menstrual membranes was made in 1842 by Ernst Heinrich Weber, and the term "membranous dysmenorrhea" was applied to the condition by Oldham and Simpson in 1846 (2). A certain resemblance to decidual tissue impressed observers more and more strongly, so that a prolonged discussion was carried on, especially in Germany, as to whether all cases of membranous dysmenorrhea were not in reality merely repeated early abortions. Only within the last thirty years have the two conditions been clearly differentiated. The first adequate histological study in the modern literature on the subject is that by Wyder (1878) (9). Von Franqué, in 1893 (23), reported five cases and made an elaborate study of the pathological anatomy. Since his article numerous isolated cases have been reported, but little new information has been added to the subject.

The most important etiological factor in the condition is a preceding endometritis, arising after child-birth, an abortion or a gonorrheal infection. In other instances there is a retroflexion or some abnormality of the appendages. A considerable number of cases, however, occur in young unmarried women, with no history of infection and with pelvic organs apparently normal on examination. There is in this group, of course, the possibility of an overlooked vaginitis in childhood, or an endometritis accompanying the exanthemata.

The clinical history is usually somewhat as follows: Menstruation was regular and normal until after a labor or an abortion followed by fever, or after a gonorrheal infection. Dysmenorrhea then developed, followed in a few months by the appearance of membranes. These may be discharged only at intervals of three or four months. Usually, however, one is passed at each period; in exceptional cases two or more. Menstruation is accompanied by pain, and the expulsion of the membrane, which usually occurs on the third or fourth day, is preceded by intermittent uterine contractions, similar to those of labor. These cease after the discharge of the membrane, which is often followed by copious hemorrhage.

The prognosis as to recovery, either with or without treatment, is not good, as the condition usually persists until the menopause. Sterility is the rule, although a few patients recover and become pregnant.

The treatment most often adopted in cases where the underlying condition is obscure, is curetting a few days before menstruation, followed by the application of tincture of iodine or carbolic acid to the uterine cavity. This procedure frequently gives temporary relief, but the patients usually relapse within a few months. Any associated lesions of the uterus or appendages should of course receive appropriate treatment.

The menstrual membrane, when discharged entire, forms a triangular sac, having the shape of the uterine cavity, and sometimes showing rounded holes at the sites of the tubal openings. The outer surface (*i. e.*, towards the uterine wall) is ragged; the inner is smooth. The thickness of the membrane varies from that of tissue paper to two or three millimeters. Membranes of greater thickness suggest decidua. Complete casts of the uterine cavity are rarer in membranous dysmenorrhea than in pregnancy, the tissue in the former condition being usually passed in fragments.

A variety of microscopic appearances have been described in this condition. The membranous discharges from the uterus may be divided, however, into two groups (excluding decidua for the present): exfoliated mucosa and fibrinous casts.

In membranes composed of altered mucosa, two pictures

may be differentiated in a general way. The first is that of an interstitial endometritis. The stroma cells are of normal size and appearance, and there is an infiltration of lymphocytes. Hemorrhage, exudate, and fibrin are usually present in addition. In the second type the stroma cells show a strong resemblance to decidua. They are enlarged, oval or polygonal in shape, with a large vesicular nucleus and abundant protoplasm. All gradations may be traced between these decidua-like forms and the normal stroma cells. The entire membrane may be composed of these altered cells, or glands may also be present. Occasionally a compact and a spongy layer can be distinguished. The two pictures—interstitial endometritis and decidua-like areas—are often seen in the same membrane. It is these enlarged stroma cells which have given rise to so much confusion and to a prolonged discussion as to whether there is any criterion by which they may be differentiated from true decidual cells. They are usually interpreted in menstrual membranes, as the result of chronic hyperæmia and irritation. They are not, however, peculiar to this condition, being found also in glandular hypertrophy and œdema of the endometrium, where they are accounted for by circulatory changes.

Most membranes show signs of degeneration, varying from a hydropic appearance of the cells and inability to take ordinary stains, to coagulation necrosis. A "budding" of the interglandular tissue has been described by Von Franqué (23) and also by Hegar and Maier; *i. e.*, compact foci of stroma cells in which growth is more active, and which penetrate independently in different directions through the loose stroma. These authors found them also in the hyperplasia of the decidua associated with hydrorrhea gravidarum. They consider it a change which may be found in any plastic inflammation.

Amyloid change in the vessel walls has been found in membranes from a case of prolonged and severe pelvic inflammation. Large numbers of eosinophiles and also mitoses in the stroma cells have been reported by several observers.

Fibrinous casts are composed of a network of fibrin containing in its meshes red corpuscles, leucocytes, and remnants of the cells of the mucosa. There is some doubt as to whether these casts should be classified with true cases of membranous dysmenorrhea. Some authors exclude them entirely. They develop, nevertheless, in connection with endometric processes, and are passed with the same symptoms as the organized membranes. In fact, cases have been reported, in which the same patient passed at one time a fibrinous cast, and at another a membrane of altered mucosa. It is impossible, also, to separate the two varieties anatomically, as many transitional forms are found between the simple fibrinous cast and the well-preserved, exfoliated endometrium. Schönheimer (22) considers the process to be an acute fibrinous inflammation occurring under the influence of menstrual congestion, after a terminated endometritis, and subsiding at the end of the period.

The mechanism of separation of the membrane is obscure. The most generally accepted theory is that the hyperplasia of the stroma cells causes an obstruction to the escape of blood into the superficial layers; hence it spreads out in the deeper portions of the mucosa. The tissue, friable because of chronic hyperæmia and its young connective-tissue cells, yields in its weakest part, and the membrane is dissected off by hemorrhage. The free bleeding which frequently follows the expulsion of the cast is thought to confirm this theory. An abnormal density in the superficial layers of the endometrium would also hinder the escape of the blood, and lead to the same result. Speaking against this mechanical theory of separation is the fact that the blood is often distributed equally through all parts of the membrane.

The degenerative changes found in the greater number of membranes must also be an important factor in causing separation,—possibly quite as important as they are in the separation of the decidua. Regressive processes in the decidua—chiefly coagulation necrosis with the appearance of fibrin—appear in the second half of pregnancy and are marked at term. The membranes from our first case show widespread coagulation necrosis in the stroma, and in the second case the process is beginning. In both cases there are pronounced changes in the blood-vessels,—many are occluded with fibrin and their walls degenerated.

The diagnosis of membranous dysmenorrhea, although it may be very probable from the clinical history, should not be made without a microscopic examination, as there are two other discharges from the genital tract, which may simulate menstrual membranes macroscopically. These are vaginal casts, or fragments of vaginal epithelium, and decidual casts. The former are thrown off, either as the result of an exfoliative vaginitis, or treatment of the vagina with strong chemicals, such as silver nitrate. The tissue in exfoliative vaginitis may be passed either during menstruation or independently of it. If the pieces are passed with pain during the period, the case may be considered one of membranous dysmenorrhea. This was the case in two specimens sent to the laboratory, with the diagnosis of "membranous dysmenorrhea," and proving, on microscopic examination to be of vaginal origin. An exfoliative vaginitis may accompany a true membranous dysmenorrhea. Leopold (11) reports a case of this kind, and considers the cause of the two processes the same, *i. e.*, a superficial hemorrhage, arising from extreme hyperæmia, and extending through the cervix into the vagina. Hoggan (6) describes a membrane, the upper part of which was composed of uterine mucosa, the lower of vaginal epithelium. If small portions of vaginal epithelium are passed together with endometrium, the former may be overlooked, in case only the larger pieces in the specimen are examined.

As a rule vaginal casts and pieces of vaginal tissue are thinner, tougher, and more parchment-like than membranes from the uterus, and no glandular openings are seen on the surface. The diagnosis can be made immediately with the microscope.

Decidual casts are expelled in abortion, extra-uterine pregnancy, and in the rare cases of pregnancy in one horn of a double uterus. The typical decidual cast is larger, thicker,

and more vascular than the dysmenorrheic membrane. If chorionic villi are found on microscopic examination, the diagnosis of intra-uterine pregnancy is of course clear. If decidua alone is present, the only diagnosis that can be made, from consideration merely of the cast, is that of the existence of pregnancy,—either in a normal uterus, a rudimentary horn, or a tube.

The greatest difficulty, however, has arisen over the differential diagnosis of an early abortion from a menstrual membrane containing large decidua-like cells. The question arises chiefly in cases of early pregnancy, before the decidua has reached its full development and typical form. Cells, which in size, form, nucleus, and staining properties closely resemble true decidual cells are found apart from pregnancy, not only in menstrual membranes, but also in œdema of the endometrium, glandular hypertrophy, and inflammatory conditions of the mucosa. There may be no difference in size between these enlarged forms and decidual cells, as was proved by Von Franqué (25) in a series of measurements; but the former do not show the epithelioid appearance found so often in the mature decidual cell, which has more abundant protoplasm and a much more sharply-defined outline. The protoplasm of the decidual cell also loses its fibrillated appearance and takes a deeper eosin stain. Although the differential diagnosis of a menstrual membrane from typical decidua is usually clear on microscopic examination, there are many confusing cases, in which the question of early pregnancy cannot be excluded without the aid of the clinical history.

There are specimens from three cases of genuine membranous dysmenorrhea in the collection of the gynecological laboratory of the Johns Hopkins Hospital, and also one specimen of a fibrinous cast, which, from the patient's history, should be included in this group.

The cases are as follows:

Case I.—L. R., age 20. Gynecological history No. 12,427. Sent by Dr. G. K. Vanderslice, Phoebus, Va. Was admitted to the Johns Hopkins Hospital, October 11, 1905, and discharged October 20, 1905.

Complaint.—Pain in left side, painful menstruation and backache.

The family history was unimportant.

Past history and present illness.—Patient has always been well, aside from the present trouble. There is no history of severe infectious diseases.

Had a tumor removed from the right breast in 1904. Menstruation began at twelve years, is regular every four weeks, lasting seven days, and has been painful and profuse from the beginning. Ever since the onset, so far as patient can remember, she has passed with each period "pieces of flesh." Dysmenorrhea is severe on the first day, less on the second, and on the third day the membrane is passed during a paroxysm of pain, lasting about one hour. This pain, which is always located a little to the left of the mid line, is sharp, and, as patient expresses it, "feels like raking over a raw surface." It is relieved immediately by expulsion of the membrane, which is sometimes followed by considerable hemorrhage; at other times none.

Patient has also less marked paroxysms of pain in the intermenstrual interval. These attacks last frequently but a few minutes, and may occur several times a day, or at intervals of several days. The pain is located in the same spot as during menstruation. Patient thinks that the pieces of membrane passed at present are smaller than formerly, and that she is gradually improving.

About a year before admission patient noticed that the uterus was situated low down, and since then she has been troubled with backache and leucorrhea.

Physical examination on entrance showed a well-nourished girl. The heart, lungs, and abdomen were normal.

Pelvic examination under ether gave the following: Outlet, virginal; no signs of infection; cervix low, 1½ in. from the outlet; fundus in anteposition; freely movable; both ovaries easily felt and apparently normal.

A dilatation and curetting were performed, and a very small amount of endometrium, normal in appearance, was obtained (nineteen days after the last period). The specimen unfortunately was not saved.

Patient made an uneventful recovery, and was discharged ten days after admission. She sent to the laboratory some material passed during the period in November, which on microscopic examination showed nothing but blood clot.[1]

The laboratory possesses three specimens from this patient, the first passed when she was fifteen years old, the second in August, 1902, at the age of seventeen, and the last in March, 1905. There is a certain similarity in the membranes, all of which show marked vascular, inflammatory and degenerative changes, and the first two also glandular hypertrophy.

The first membrane (gyn. path. No. 8315), has been imperfectly preserved and stains poorly. Surface epithelium is absent. The glands, which run parallel to the surface, are irregularly distributed. In the upper half of the membrane they are scarce, and lacking altogether in large areas. In the lower part of the membrane, however, they are increased in number, and in some places form a tortuous mass, separated by only scanty stroma. The epithelium is sometimes reduplicated and projects into the lumen in the form of tufts. The dilated lumina contain desquamated epithelium; red corpuscles and fibrin.

Fig. 1.—Case I. Gyn. Path. 8315. Showing glandular changes and areas of beginning necrosis in stroma.

The stroma cells are not increased in size, and aside from a degenerated appearance, due partially to the poor preservation, show no abnormality. Small areas of beginning necrosis, from which networks of fibrin radiate, are scattered through the

[1] A letter from patient's physician dated April 15, 1906, states that she is again passing membranes, but with less pain.

stroma. The blood-vessels are numerous and comparatively large. Some are filled with well preserved red corpuscles; others with fibrin. Shadows of red cells are found throughout the tissue; also numerous leukocytes.

The membrane passed in August, 1902 (gyn. path. No. 8399), consists of a piece of tissue about 3 mm. thick, and approximately the size and shape of the uterine cavity. Microscopically it presents a striking picture, on account of the marked glandular hypertrophy and the extensive degenerative changes.

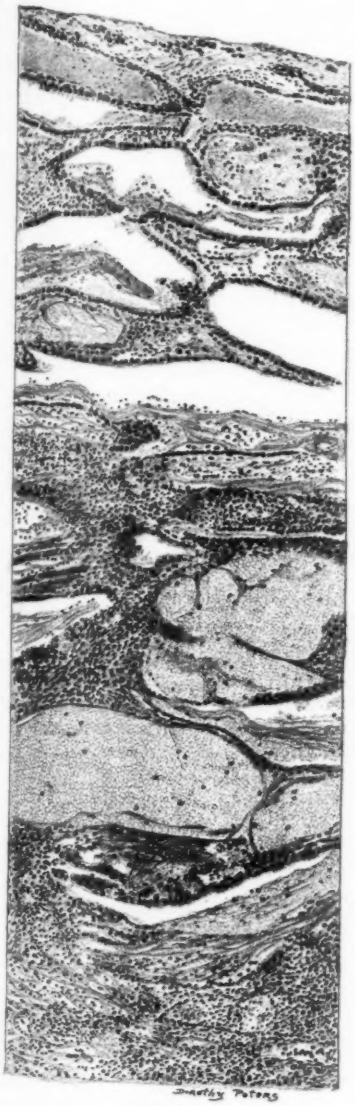

FIG. 2.

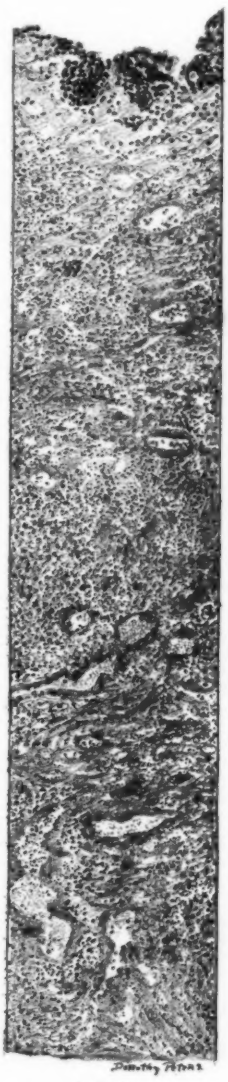

FIG. 3.

FIG. 2.—Case I. Gyn. Path. 8399. Section through entire thickness of membrane, showing glandular dilatation, changes in blood vessels and degeneration in stroma.

FIG. 3.—Case I. Gyn. Path. 8400. Section through entire thickness of membrane, showing extensive necrosis and changes in blood vessels.

The surface epithelium is mostly lacking, being represented only by a few groups of cuboidal cells. The stroma immediately beneath the surface is thickened, and contains compressed and atrophied glands, which run parallel to the surface. In the deeper portions of the membrane are groups of tortuous and greatly dilated glands. They are lined with a single layer of low-cylindrical epithelium, and their lumina are filled with fibrin, red cells and leukocytes. In the neighborhood of these glands are numerous very large thin-walled vessels distended with blood. The stroma cells are somewhat enlarged. In a few areas near the large blood-vessels they stain clearly. For the most part, however, the cell outline and nucleus are indistinct and stain faintly and diffusely. Many of the cells are swollen. Some nuclei are shrunken and take an intense stain; others are undergoing fragmentation. The stroma cells are widely separated by fresh hemorrhage and exudate, and there is everywhere an abundant network of fibrin and a thick infiltration with polymorphonuclear leucocytes. The blood-vessels are numerous and large. Many are filled with fibrin and the walls of some of the smaller stain homogeneously with eosin, as if undergoing hyaline change.

The membrane expelled in March, 1905 (gyn. path. No. 8400), shows more advanced degenerative changes than the preceding. It is composed of thickened stroma, showing areas of coagulation necrosis, especially in the region of the blood-vessels. Clinging to the edges of the membrane are fragments of well preserved glands and stroma. The cells of the membrane are somewhat larger than normal. They all stain diffusely, are indistinct in outline, and show shrinking or fragmentation of their nuclei. The blood-vessels, which are numerous in the deeper portions of the tissue, show marked degeneration, their walls stain homogeneously with eosin, and their lumina are filled with fibrin. The entire membrane is traversed with a network of fibrin and thickly infiltrated with polymorphonuclear leukocytes.

CASE II.—The membrane from this case was sent to the laboratory February 7, 1905, by Dr. J. B. Beeson, of Livingston, Montana, with the following history: The patient, age 30, is a well-formed, healthy-appearing woman, married five years. Her menstrual history was normal until the appearance of the membranes. She had one or two abortions (probably artificially induced), during her early married life; for the past two or three years, she has not been pregnant. She began to pass membranes eight or nine months ago, and since then has discharged one at each period. Severe dysmenorrhea, confining her to bed for two or three days, developed coincidently with the appearance of the membranes. No pelvic examination was made and the patient has been lost sight of.

The specimen (gyn. path. No. 8239), consists of a few shreds of grayish-red tissue. Microscopically it is composed almost entirely of stroma. The surface epithelium is absent, and only an occasional remnant of a gland is seen. The stroma varies much in density; the cells in some areas being more closely set than normal; in others separated by exudate and their character changed. The rarified areas are, as a general rule, near the free surface of the membrane; the denser areas in the interior, where they occasionally surround the blood-vessels. The largest of the altered stroma cells have round, vesicular, faintly staining nuclei, two or three times the size of those of the usual stroma cells. The cell outline cannot be defined; but the protoplasm is small in amount and stains very faintly with eosin. Every gradation can be traced between them and the normal stroma cell. Numerous thin-walled vessels are present throughout the section, most of them occluded with fibrin. From them a delicate network of fibrin spreads out into the surrounding tissue. Indeed, the abundance of fibrin, both within and without the vessels is a striking feature. Scattered everywhere throughout the membrane are foci, in which the fibrinous network and the leucocyte infiltration are denser, and the stroma cells are indistinct and stain diffusely. In a few

places the process has advanced to actual necrosis. There is everywhere a marked infiltration with small round cells, especially about the thrombosed vessels.

Even in the absence of a pelvic examination, both the clinical history and microscopic appearance of the membrane point to an inflammatory origin in this case.

Case III.—The following history is obtained from Dr. C. D. McLeod, of Chatfield, Ohio, who sent the specimen to the laboratory. The patient, age 38, was married at 16 years of age, and has four children. No history of puerperal infection. She has had marked dysmenorrhea for the past seven years, and during the last two or three years has passed shreds of membrane. She has also been subject to severe pain in the pelvis about ten days after menstruation. About twelve years ago she had some nervous trouble, diagnosed as "cerebro-spinal meningitis," which has left her with a partial paralysis of the left side.

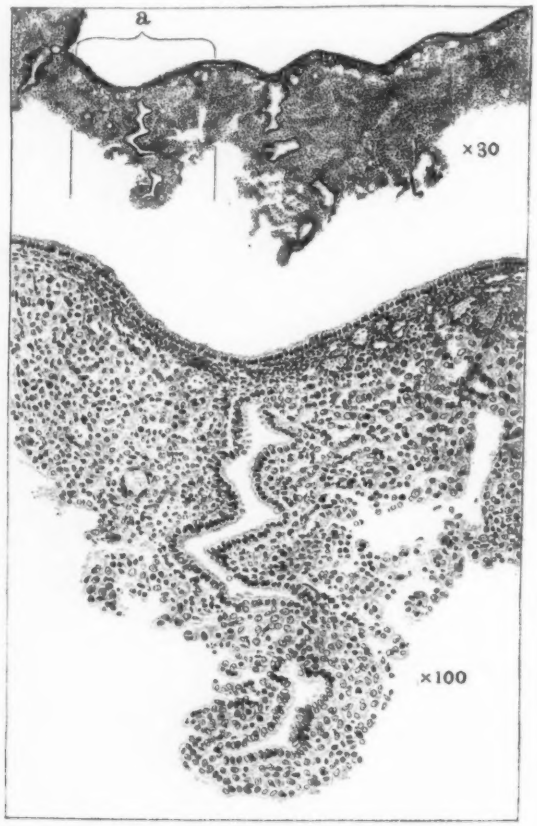

Fig. 4.—Case III. Gyn. Path. 8648. Showing enlarged stroma cells. (Drawn by Miss Young.)

The physician when called to the patient in November, 1904, found her having alarming hemorrhage and severe intermittent pains. He removed a complete cast of the uterus (the present specimen), which he took at the time to be an abortion sac. Pelvic examination showed a prolapsed, enlarged and softened uterus. The two periods following this one were also attended by profuse hemorrhage. The patient then improved temporarily, and would pass two or three periods without discharging membranes. She has relapsed since, however, and membranes have again appeared.

The specimen (gyn. path. No. 8648), is composed of the upper portion of the endometrium, about 1 mm. in thickness, and gives the impression of having been separated en masse. The appearance is perhaps due partially to the fact that manual aid was given in the removal of the cast. The inner surface is smooth and the epithelium fairly well preserved. The surface towards the uterine wall is ragged and shows parts of glands, some of them abruptly torn across, projecting beyond the stroma. The glands are convoluted and dilated. Their epithelium shows no abnormality. The stroma is denser towards the surface; in the lower layers separated by exudate. The cells are considerably enlarged, oval or stellate in outline, and have a round, pale-staining nucleus and an increased amount of protoplasm. Many have a swollen and hydropic appearance. They are pushed apart by serous exudate and in some areas by a small amount of hemorrhage. Numerous lymphocytes are scattered everywhere throughout the membrane. The blood-vessels are abundant, and are filled with well-preserved red cells. The degenerative changes and fibrin, so conspicuous in the other membranes, are absent in this specimen.

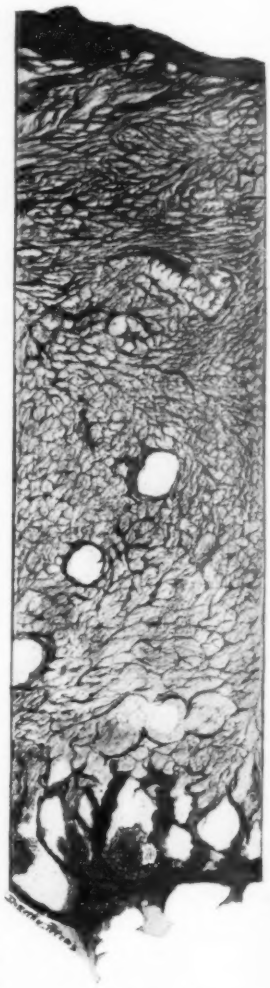

Fig. 5.—Case IV. Gyn. Path. 8470. Section through fibrinous cast from uterus.

Case IV.—There is in the gynecological laboratory only one example of fibrinous cast of the uterus. This was sent by Dr. E. C. Seufert, of Chicago, with the following history: M. S., single, age 24. Born in Poland and came to America at the age of 18. Has worked in tailor-shops for the past five years.

Had diphtheria and scarlet fever at about eight years of age, with perfect recovery from both. She was very stout at the time of puberty. Menstruation began at thirteen and was irregular for several years. The flow has been slight, lasting for three days, and from the onset accompanied by dysmenorrhea. The pain has increased in severity, and on the third or fourth day of each period during the last three years she has passed stringy mucous and shreds of membrane. No leucorrhea.

Patient consulted the physician in January, 1905, for the increasing dysmenorrhea. She brought with her a complete fibrinous cast of the uterus,—the first one which had been expelled entire.

Physical examination at that time showed the patient to be well-nourished, and the chest and abdomen negative. The uterus was normal in size and position, and movable. Patient refused the treatment recommended, and it has been impossible to trace her subsequent history.

The specimen from the cast (gyn. path. No. 8470), shows mi-

croscopically a heavy, loose-meshed network of fibrin, in which remnants of cells are in places visible. There is a wide band of fibrin on the surface; below that a layer of finer network; and in the lowest stratum are numerous rounded openings, some of which are artefacts, and others of which seem to have been blood-vessels. The cells which are scattered throughout the network are so degenerated that no idea of their nature can be obtained.

In conclusion I must express my gratitude to Dr. Howard Kelly, who suggested the subject for this paper; to Dr. Elizabeth Hurdon for her constant help and interest; to Mr. Max Broedel for superintending the illustrations; and to the physicians in charge of the cases for their courteous and detailed replies to numerous letters.

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THE MEDICAL LIFE OF OLIVER WENDELL HOLMES.[1]

By J. H. MASON KNOX, JR., M. D.

The birth of Oliver Wendell Holmes into the medical world was hardly a spontaneous one, but was rather the result of a protracted labor and took place after a long period of uncertainty and doubt.

At the age of nineteen, when a junior at Harvard, he writes to his boyhood's friend, Phineas Barnes, that he is totally undecided what to study; "it will be law or Physic, for I cannot say that I think the trade of authorship adapted to this meridian."

While at college Holmes showed in formation many of the convivial charms that so graced his later life. He was popular, the center of much of the social life of his class, and was often called upon at various society and class functions to exercise his ready rhyming pen in descriptive verse. He contributed several articles to the college magazine, the "Collegian." It was here he suffered, as he said, his first attack of "author's lead poisoning."

His father, a clergyman of rather liberal views and latitude for that period seems to have interposed no serious objections to the moderate indulgence of his son's convivial proclivities.

His mother was Sarah Wendell, a sprightly and lovable woman, from whom Holmes inherited many of his genial traits.

He describes himself at college as a "plumeless biped of exactly five feet three inches when standing in a pair of substantial shoes, having eyes which I call blue." "I am rather lazy than otherwise, and certainly do not study as hard as I ought to. I am not dissipated and I am not sedate. I stood at the humble rank of 17th scholar." He graduated in June, 1829, in a class noted for its high character, and which then and for many years afterwards made Holmes the center of their yearly reunions, which he often celebrated in verse.

After this came the well-known period of doubt as to his work. He studied law for a year, but never seems to have liked it. We find him writing in a few months to a friend: "I am sick at heart of this place (the law school) and at almost everything connected with it. I know not what the temple of the law may be to those who have entered it, but to me it seems very cold and cheerless about the threshold."

So after the first year he entered the Harvard Medical

[1] Much of material for this sketch was obtained from the "Life and Letters of Oliver Wendell Holmes," edited by John T. Morse, Jr., 1896.

School September 30, 1830, at the age of twenty-one, and began the studies which brought him contentment and influenced all his later life. He writes to Barnes shortly after his "flop" to medicine: "I must announce to you the startling proposition that I have been a medical student for more than six months and am sitting with a stethoscope on my desk and the blood-stained implements of my profession about me. I know I might have made an indifferent lawyer; I think I may make a tolerable physician. I did not like the one, I do like the other, and so you must know that I have been going to the Massachusetts General Hospital and slicing and slivering carcasses of better men and women than I ever was or am like to be. It is a sin for a puny little fellow like me to mutilate one of your six-foot men as if he were a sheep, but 'vive la science.'"

Little is recorded of Holmes' life at the medical school. Undoubtedly he soon came under the influence of that great clinician and teacher, Dr. James Jackson, who was Professor of the Theory and Practice of Medicine from 1812-1846, and whose son was but a little further on in his medical studies. Dr. Jackson had studied in England and knew the value of the wider experience at the European clinics, and it may well have been at his suggestion that Holmes decided to go abroad and continue his medical education in Paris, which at that time and for a quarter of a century afterwards was the Mecca which all ambitious followers of the healing art sought to reach.

This French nursing converted the weak and underfed medical infant, whose birth had been attended with so many fears, into a sturdy, self-reliant child, able to sit up and take the strong diet of the many clinics and to do some vigorous, independent thinking.

Holmes was associated with a distinguished group of American students, among whom may be mentioned Jackson and Bigelow, Hooper, Warren, Gerhardt, and Morse. They lived in the Latin Quarter and attended the lectures and demonstrations of such men as Louis and Andral, Dupuytren and Larry, who were leading the medical world of their day.

Holmes reached Paris April, 1833, and soon after was completely absorbed in his work. After a few months he writes: "I am more and more attached to the study of my profession and more and more determined to do what I can to give to my own country one citizen among others who has profited somewhat by the advantages offered him in Europe. The whole walls of the Ecole de Médecine are covered with notes of lectures, the greater part of them gratuitous. . . . The dissecting rooms are open and the lessons are ringing aloud through all the great hospitals."

He usually began the day at seven o'clock at the hospital of La Pitié, where he attended lectures and clinics until breakfast at about eleven, after which he studied until 5 p. m., when he often dined at some "café" with a company of his fellow students. He speaks approvingly of the tasteful viands and the pleasing wines, very different from the "crude joints, the massive puddings, the depressing pies, and the hard cider which marvelously nourished New England in its era of development."

The period spent by Holmes in Paris was part of an epoch of remarkable progress in the history of medicine. The short but brilliant researches of Bichat had shown the close relationship between symptoms of disease and definite anatomical conditions and had dissipated many of the philosophical and visionary theories which had been thought sufficient to explain the phenomena of illness.

Following this with the work of Corvesart and Laennec, came the introduction of accurate methods of diagnosis by percussion and auscultation and the insistance by Louis of the statistical method of study; that deductions concerning a diseased state should be made only after carefully tabulating many similar conditions and not from a single instance.

This great teacher, who was just in his prime while Holmes was in Paris, was undoubtedly the most inspiring personality felt by the large group of American students. "Louis had," he writes, "in a rare degree the power of attracting youth, so that those who followed him among the beds of the hospitals became filled with an ardent ambition. He was the object of our reverence, I might almost say of idolatry; modest in the presence of nature, fearless in the face of authority, unwearying in the pursuit of truth, he was a man whom any student might be happy and proud to claim as his teacher and friend." Holmes, apparently was admitted, at least during his second year, to some degree of intimacy with Louis. He writes that he had constant access to two wards containing one hundred beds where he can examine patients and that on one occasion at least he had a "tête-à-tête dinner with his great teacher who intrusted to him the analysis of a work which he is going to make use of in a publication."

He became a member of the Society of Medical Observation, of which Louis was perpetual president and which was devoted to the discussion of important cases and the presentation of new work.

Other luminaries whose path he crossed during the precious time abroad he mentions, particularly in his delightful valedictory address to his class at the Harvard Medical School.

He did not have much to do with Andral who, although then a young man, was rapidly rising in fame and overshadowing the passing greatness of Broussais, whose "theories of gastro-enteritis as the cause of disease ran over the field of medicine like flame over the grass of a prairie, and who was in those days like an old volcano which has pretty nearly used up its fire and brimstone but is still boiling and bubbling in its interior and now and then sends up a spirit of lava and a volley of pebbles."

Of the intrepid men who operated in Paris in those ananesthetic days, Holmes recalled particularly Lisfranc, whom he describes as a "great drawer of blood and hewer of members and who regretted the splendid guardsmen of the old Empire because they had such magnificent thighs to amputate."

Then there was the short, square, substantial man with iron-grey hair, ruddy face, and white apron. This was Baron Larry, Napoleon's favorite surgeon. He was still strong and

sturdy; he adds, "few portraits remain printed in livlier colors on my memory." "To go around the Hôtel des Invalides with Larry was to live over again the Campaigns of Napoleon, to the last charge of the Red Lancers in the redder field of Waterloo."

He visited frequently l'Hôtel Dieu, where ruled and reigned the Master Surgeon of his day, the illustrious Baron Dupuytren. "No man disputed his reign, some envied his supremacy. He marched through the wards like a lessor kind of deity."

He mentions also the vivacious Ricord, whom he called the "Voltaire of Pelvic literature; a skeptic as to the morality of the race in general, who would have submitted Diana to treatment with his mineral specifics and ordered a course of blue pills for the vestal virgins."

His time was not spent altogether in work, for he speaks of quite a list of renowned actors and singers and dancers who contributed to his recreation. He delighted to roam about the streets of Paris at night in looking at the shops which he thinks "greatly superior to those of Boston." He took especial pleasure in hunting for old books on the walls of the "Quais" and at the small dealers. He was present at the dinner among the Americans on July 4, 1833, which was also graced by "that inextinguishable old gentleman, Lafayette."

He was in a dreadful state of anxiety lest he should have to come home after his first year. He seems to have been a considerable drain upon the resources of his good parents, as Holmes, although not extravagant, was not willing to live meanly. He was known as a good dresser. He would come home if he must but he was "not willing to eat a dinner for twenty-five sous and drink sour wine at a cheap restaurant."

However, after several importunate letters he persuaded his father that a "boy is worth his manure as well as a potato patch" and embarked on his second year's work with renewed energy.

In the spring of his second year, with a Swiss who had known successively Jackson and Bowditch, Holmes took a course in operative surgery at a morgue in connection with a large cemetery. "Here at 12 noon every day," he narrates, "you might have seen M. Bizot and myself, like the old gentlemen at market, choosing our day's provisions with the same epicurean nicety. We paid fifty sous a piece for our subject and before evening we had him cut into inch pieces." "In England and America," he says, in contrast, "one may dissect but rarely operate upon the subject."

Holmes spent the summers, after the close of the lectures, in travel. In 1834, with several companions, he visited the Rhine Provinces, the low countries, and England. In London he saw something of the hospitals, but was not weaned from Paris as the city of his choice.

In July, 1835, he packed his accumulated belongings, a select little professional library, a modest stock of instruments, two skeletons and some skulls, and in the autumn, after an extended tour in Switzerland and Italy, he returned home, landing in New York in December. I have dwelt, perhaps, unduly upon the foreign experiences of Dr. Holmes, but it seems to have exerted a controlling influence upon all his subsequent professional life.

He returned to America with high ideals, with well-developed powers, a large amount of professional knowledge and skill, a self-reliance, an independence of thought, and a store of pleasant and useful memories which formed a part of his life's equipment through all the succeeding years.

In 1836 he took his degree of Doctor of Medicine from Harvard University and immediately started to practice. He shortly joined the Massachusetts Medical Society. In actual practice he seems to have had only moderate success. It is doubtful if he ever cared much for the life of a general practitioner. And he admitted that he did not make any strenuous efforts to build up a practice. Probably he did not add many to his list of patients by publishing a book of youthful poems just a year after his return from Europe. He competed successfully for the Boylston Prize in 1836 and 1837, winning three out of the four prizes offered by writing dissertations on "Indigenous Intermittent Fever in New England," "Neuralgia," and "The Utility and Importance of Direct Oral Examination in Medical Practice." The first of these is still a medical classic. In it Dr. Holmes displayed his accurate historical sense and has gathered together all that is known of malaria, its distribution, symptoms, etc., in the early settlement of New England.

In 1838 he was appointed Professor of Anatomy and Physiology in Dartmouth College at Hanover, but resigned after a year or two. He was married in 1840 to Miss Amelia Lee Jackson, a niece of his old preceptor. Dr. Holmes, in addition to his writings, together with three friends, engaged in teaching at the Tremont Street Medical College, a kind of supplementary institution to the Harvard Medical School, and in association with Dr. Bigelow he edited the American edition of Marshall Hall's text-book on the Theory and Practice of Medicine.

In 1842 he published two lectures on "Homeopathy and its Kindred Delusions." In them various senseless medical fads are playfully reviewed. The reader is introduced to the Royal cure of the King's Evil, the Weapon Ointment, which was applied to the weapon producing the wound for its healing, the Tar Water Mania of Bishop Berkely, and the "metallic tractors" of Mr. Perkins. Homeopathy, which he had doubtless become familiar with in Paris, is discussed in no stinted language in the second lecture. The good doctor hated homeopathy with a whole-souled hatred. He spoke of it as a "pseudo science." He showed its inconsistencies and absurdities. The argument founded on its occasional good results would be just as applicable, he said, to the counterfitter who gives base coin on the ground that a spurious dollar had often relieved a poor man's necessities.

The parallel which the homeopathists attempted to draw between the effects of their infinitesimal doses and the production of small-pox from minute quantities of animal vaccine he shatters with the suggestion that the mind advancing this argument could reason that "a pebble may produce a mountain because an acorn can become a forest, or that because a

spark will burn down a city a mutton-chop will feed an army."

He refers to the absurdity of the original contention of Hahnemann, the founder of the cult, that seven-eighths of all chronic diseases are the result of psora, a skin affection called the itch.

He points out that to show the axiom "Similia Similibus Curantur" (like is cured by like) to be the sole law of nature in therapeutics, it is necessary to establish that drugs are always capable of curing diseases most like their own symptoms and that remedies should be shown not to cure diseases when they do not produce symptoms resembling those presented in these diseases. Neither of these propositions has ever been established. He predicts that the "Semi-Homeopathist will gradually withdraw from the 'rotten half of his business and try to make the public forget his connection with it and the ultra-Homeopathists will either recant or embrace some new and equally extravagant doctrine'; very few will stick to their colors and go down with their sinking ship."

Unquestionably Dr. Holmes' most important contribution to medicine was made in 1843, when he read before the Boston Society for Medical Improvement an essay on the Contagiousness of Puerperal Fever. This was published in the New England Quarterly Journal of Medicine and Surgery for April of that year. The journal soon ceased to be published and the essay can hardly be said to have been brought before the profession.

It must be recalled that this was long before the days when the nature of contagion was understood and several years before the extended researches of Semmelweis[2] on the same subject. Holmes, in his original essay, which he republished unchanged twelve years later, marshals a startling number of cases of puerperal fever presumably carried to the mother by the attending physician or nurse. He points out clearly the probable connection between erysipelas and child-bed fever. His contention met with violent, almost contemptuous opposition from the leading obstetricians of the day, notably by Drs. Hodge and Meigs, of Philadelphia. The latter wrote in 1852: "I prefer to attribute these cases to accident or Providence, of which I can form a conception, than to a contagion of which I cannot form any clear idea"; and Hodge advises his students to "divest their minds of the overpowering dread that you can ever become the minister of evil, that you can ever convey in any possible manner a horrible virus so destructive in its effects and so mysterious in its operations as that attributed to puerperal fever."

In republishing the essay in 1855, Holmes makes an earnest plea to students for freedom from the trammels of authority, for individual judgment of facts. "Students," he says, "have naturally faith in their instructors, turning to them for truth and taking what they may choose to give them: babes in knowledge, not yet able to tell the breast from the bottle, pumping away for the milk of truth at all that offers were it nothing better than a professor's shrivelled forefinger."

The rules for the guidance of physicians in midwifery practice laid down by Holmes in 1843 need little revision to-day:

"1. A physician holding himself in readiness to attend cases of midwifery should never take any active part in the post-mortem examination of cases of puerperal fever.

"2. If a physician is present at such autopsies, he should use thorough ablution, change every article of dress, and allow twenty-four hours or more to elapse before attending to any case of midwifery. It may be well to extend the same caution to cases of simple peritonitis.

"3. Similar precautions should be taken after the autopsy or surgical treatment of cases of erysipelas, if the physician is obliged to unite such offices with his obstetrical duties, which is in the highest degree inexpedient.

"4. On the occurrence of a single case of puerperal fever in his practice, the physician is bound to consider the next female he attends in labor, unless some weeks at least have elapsed, as in danger of being infected by him, and it is his duty to take every precaution to diminish her risk of disease and death.

"5. If within a short period two cases of puerperal fever happen close to each other, in the practice of the same physician, the disease not existing or prevailing in the neighborhood, he would do wisely to relinquish his obstetrical practice for at least one month, and endeavor to free himself by every available means from any noxious influence he may carry about with him.

"6. The occurrence of three or more closely connected cases, in the practice of one individual, no others existing in the neighborhood, and no other sufficient cause being alleged for the coincidence, is prima facie evidence that he is the vehicle of contagion.

"7. It is the duty of the physician to take every precaution that the disease shall not be introduced by nurses or other assistants, by making proper inquiries concerning them, and giving timely warning of every suspected source of danger.

"8. Whatever indulgence may be granted to those who have heretofore been the ignorant causes of so much misery, the time has come when the existence of a private pestilence in the sphere of a single physician should be looked upon, not as a misfortune, but a crime; and in the knowledge of such occurrences the duties of the practitioner to his profession should give way to his paramount obligations to society."

The earnestness of the writer, to whom hundreds of mothers owe their lives, is attested by the closing paragraphs of the original paper:

"The woman about to become a mother, or with her newborn infant upon her bosom, should be the object of trembling care and sympathy wherever she bears her tender burden, or stretches her aching limbs. The very outcast of the streets

[2] J. P. S. Semmelweis was born in 1818, and graduated in Medicine in 1846. Shortly after this time he became interested in the study of Child-bed fever. He probably considered it contagious as early as 1849, and defended his contentions in numerous personal letters, written between 1858 and 1860. His first formal publication on the subject, entitled: "Die Aetiologie der Begriff und die Prophylaxis des Kindbettfiebers," appeared in 1861.

has pity upon her sister in degradation, when the seal of promised maternity is impressed upon her. The remorseless vengeance of the law, brought down upon its victim by a machinery as sure as destiny, is arrested in its fall at a word which reveals her transient claim for mercy. The solemn prayer of the liturgy singles out her sorrows from the multiplied trials of life, to plead for her in the hour of peril. God forbid that any member of the profession to which she trusts her life, doubly precious at that eventful period, should hazard it negligently, unadvisedly, or selfishly!"

In the "Professor at the Breakfast Table," he said, "I held up to the professional public the damnable facts connected with the conveyance of poison from one young mother's chamber to another's, for doing which humble office I desire to be thankful that I ever lived, though nothing else good should ever come into my life."

Holmes' graceful pen was soon recognized and he was asked to lecture, much to his personal inconvenience, in the many towns about Boston. He kept up his interest in medical history and practice, however, and gave some instruction in the use of the microscope, which instrument he was among the first to use in this country. He had unusual mechanical skill and was interested in the adjustment of the lens almost as much as in the study of the specimen, although he did describe some cells at the ends of long bones in a paper which he read at a medical gathering in 1851. Later he invented a stereoscope for hand use, described as an exceedingly clever device, which if patented might have made him for those times a rich man.

In 1847, at the age of 38, Holmes was elected Professor of Anatomy and Physiology at Harvard Medical School, which position he held continuously for thirty-five years, although the Chair of Physiology was separated in 1871.

As a lecturer in anatomy Holmes became immediately popular. He knew his subject well and loved it, and was able to enliven his lectures with witty allusions which fixed the object in the students' memory. "Gentlemen," he said on one occasion, holding up a female pelvis, "this is the triumphal arch under which every candidate for immortality has to pass." Again, "These, gentlemen," pointing to the lower portion of the pelvic bones, "are the tuberosities of the ischia, on which man was designed to sit and survey the works of Creation."

His lecture-room was in an old building and to reach it Holmes had to climb up a pair of dark, winding stairs, often, because of his asthma, with the help of the janitor.

He lectured five times a week during the session at one o'clock, after the students had had previously four weary hours of continuous talk. Holmes was the only one who could interest them during the last hour.

Dr. Chever, one of his demonstrators, thus vividly describes the scene, so familiar to his students, but strange to those who only knew Holmes as the writer of graceful English:

"It nears one o'clock, and the close work in the demonstrator's room in the old Medical School in North Grove Street becomes even more hurried and eager as the lecture hour in anatomy approaches. Four hours of busy dissection have unveiled a portion of the human frame, insensate and stark, on the demonstrating-table. Muscles, nerves, and blood-vessels unfold themselves in unvarying harmony, if seeming disorder, and the 'subject' is nearly ready to illustrate the lecture. . . . The room is thick with tobacco smoke. The winter light, snowy and dull, enters through one tall window, bare of curtain, and falls upon a lead floor. The surroundings are singularly barren of ornament or beauty, and there is naught to inspire the intellect or the imagination, except the marvellous mechanism of the poor dead body, which lies dissected before us, like some complex and delicate machinery whose uses we seek to know.

"To such a scene enters the poet, the writer, the wit, Oliver Wendell Holmes, and asks, 'What have you for me to-day?' and plunges, knife in hand, into the 'depths of his subject,'—a joke he might have uttered. Time flies, and a boisterous crowd of turbulent Bob Sawyers pours through the hall to his lecture-room, and begins a rhythmical stamping, one, two, three, and a shout, and pounding on his lecture-room doors. A rush takes place; some collapse, some are thrown headlong, and three hundred raw students precipitate themselves into a bare and comfortless amphitheatre. Meanwhile the professor has been running about, now as nimble as a cat, selecting plates, rummaging the dusty museum for specimens, arranging microscopes, and displaying bones. The subject is carried in on a board; no automatic appliances, no wheels with pneumatic tires, no elevators, no dumb-waiters in those days. The cadaver is decorously disposed on a revolving table in the small arena, and is always covered, at first, from curious eyes, by a clean, white sheet. Respect for poor humanity and admiration for God's divinest work is the first lesson and the uppermost in the poet-lecturer's mind. He enters, and is greeted with a mighty shout and stamp of applause. Then silence, and there begins a charming hour of description, analysis, simile, anecdote, harmless pun, which clothes the dry bones with poetic imagery, enlivens a hard and fatiguing day with humor, and brightens to the tired listener the details of a difficult though interesting study. We say tired listener because—will it be believed?—the student is now listening to his fifth consecutive lecture that day, beginning at nine o'clock and ending at two; no pause, no rest, no recovery for the dazed senses, which have tried to absorb Materia Medica, Chemistry, Practice, Obstetrics, and Anatomy, all in one morning, by five learned professors. One o'clock was always assigned to Dr. Holmes because he alone could hold his exhausted audience's attention.

"As a lecturer he was accurate, punctual, precise, unvarying in patience over detail, and though not an original anatomist in the sense of a discoverer, yet a most exact descriptive lecturer; while the wealth of illustration, comparison, and simile he used was unequalled. Hence his charm; you received information, and you were amused at the same time. He was always simple and rudimentary in his instruction. His flights of fancy never shot over his hearers' heads. 'Iteration and reiteration' was his favorite motto in teaching.

"And how he loved Anatomy! as a mother her child. He

was never tired, always fresh, always eager in learning and teaching it. In earnest himself, enthusiastic, and of a happy temperament, he shed the glow of his ardent spirit over his followers, and gave to me, his demonstrator and assistant for eight years, some of the most attractive and happy hours of my life."

Holmes took the liveliest interest in the Medical School. He was Dean from 1847 to 1853. He was always accessible to the students and ready to give them kindly counsel.

He never was a strict disciplinarian and confessed that when he examined a man who was to live on 25-cent fees he usually confined his questions to the biceps.

President Eliot said of Holmes at a Congratulatory Breakfast: "He was one of the most active and hard-working of our lecturers. I never knew any other mortal exhibit such enthusiasm over an elegant dissection. Perhaps you think it is with the pen that Dr. Holmes is chiefly skillful. I assure you he is equally skillful with the scalpel and microscope. He knows every bone, muscle, artery, and nerve, and describes them with fascinating precision. Traces of his life work occur on every page of his writings."

During Holmes' connection with the school there was a violent discussion in the faculty as to the advisability of admitting women students. He took no decided stand at the time, but later in an address made certain remarks which were probably his views on this interesting topic.

A short time afterward, when the smoke of this battle was lifting, if not quite all gone, at the opening of the new building of the Harvard Medical School, Dr. Holmes delivered an address, and Professor Dwight told the following anecdote:

"On this occasion, after speaking in his most perfect style on woman as a nurse, with a pathos free from mawkishness which Dickens rarely reached, he [Holmes] concluded: 'I have always felt that this was rather the vocation of woman than general medical, and especially surgical, practice.' This was the signal for loud applause from the conservative side. When he could resume he went on: 'Yet I myself followed the course of lectures given by the young Madame Lachapelle in Paris, and if here and there an intrepid woman insists on taking by storm the fortress of medical education, I would have the gate flung open to her, as if it were that of the citadel of Orleans and she were Joan of Arc returning from the field of victory.' The enthusiasm which this sentiment called forth was so overwhelming, that those of us who had led the first applause felt, perhaps looked, rather foolish. I have since suspected that Dr. Holmes, who always knew his audience, had kept back the real climax to lure us to our destruction."

He said he was willing to teach women anatomy but not in the same classes or dissecting-rooms with men.

Few members of the profession have been so well versed in medical literature as was Dr. Holmes. He knew the worthies and their writings from Hippocrates down. He said on presenting his loved collection of one thousand volumes and many pamphlets to the Boston Medical Library, an institution largely due to his name and influence, and of which he was president for thirteen years: "These books were very dear to me as they stood on my shelves. A twig from some one of my nerves ran to every one of them." A visitor at his home describes his joy when a copy of the original edition of Vesalius came from New York. He was fond of showing to agents for new anatomical books how superior were the illustrations in the works of some of the old writers.

When James Russell Lowell became editor of the Atlantic Monthly in 1857 he persuaded Dr. Holmes to contribute. This resulted in the Autocrat of the Breakfast Table, which immediately placed the author in the first rank of writers of sprightly English.

His literary prominence and the establishment at about the same time of the famous Saturday Club, which included among its members Emerson, Hawthorne, Whittier, Longfellow, Lowell, and Motley, gradually absorbed more and more of Holmes' interest and time.

The demands upon his muse were incessant, but were for the most part complied with. Literature, however, never really weaned him from the science of medicine, although it put a conclusive end to his practice as a physician.

As the years went by Dr. Holmes was called upon to make many addresses on occasions before medical meetings and various classes of medical students. These addresses for the most part have been gathered together in his volume of Medical Essays. They show the richness of his scholarship and his familiarity with a great variety of scientific topics and with all his kindliness and common sense.

He was a strong believer in expectant treatment, or at least in moderate and definite therapeutics, and in the self-limitation of disease as championed by Dr. James Jackson. "The traditional idea," he declares, "of always poisoning out disease as we smoke out vermin is now seeking its last refuge."

"Young man," he asks, "are you sure you cured your patient? if so, perhaps to-morrow you may kill—but then you say the patient died."

"From the time of Hippocrates," he adds, "to that of our own medical patriarch there has been an apostolic succession of wise and good practitioners who place before all remedies the proper conduct of the patient."

The assertion in a lecture on Scholastic and Bedside Teaching delivered in 1867, that the most essential part of a student's instruction is obtained not in the lecture-room but at the bedside, sounds strangely familiar, and comes with good grace from a lifelong lecturer.

His address on "the young practitioner," delivered to the class leaving Bellevue in 1871, deserves to be repeated each year to the graduate of all our medical colleges.

The influence of his professional training was exerted not only in these dissertations but permeated every page he penned. He wrote, he asserted, "medicated novels" and medical terms are frequent in his writings.

"A laugh at an entertainment," he says, "broke out prematurely. It was a sporadic laugh and did not become epidemic."

His interest in psychological problems in the power of

heredity and its effect on moral responsibility, appear in many of his works.

The scriptural limit of three score years and ten Dr. Holmes vivifies in these familiar words:

"Our brains are seventy year clocks. The Angel of Life winds them up once for all, then closes the case and gives the key to the Angel of Resurrection. Tic tac! tic tac! go the wheels of thought; our will cannot stop them; they cannot stop themselves; sleep cannot still them; madness only makes them go faster; death alone can break into the case, and, seizing the ever-swinging pendulum, which we call the heart, silence at last the clicking of the terrible escapement we have carried so long beneath our wrinkled foreheads."

Oliver Wendell Holmes stood as a constant protest against the depicting of gross and suggestive quasi-medical scenes in literature. He said that when "Zola and his tribe crossed the borders of science into its infested regions, leaving behind them the reserve and delicacy which the genuine scientific observer never forgets, they disgust even those to whom the worst scenes are too wretchedly familiar."

On retiring from his active teaching in 1882, his thought was not to rest but to devote his time more continuously to writing. He said in a letter that he "had taken off his professor's gown and was in his literary shirt sleeves." Apparently he never again gained the heights reached in the heyday of his genius, but he still wrote acceptably and with much of his old brightness to a large company of appreciative readers.

In 1886, in company with his daughter, Holmes made a hurried trip to Europe, the first since his student days more than a half-century before. His journey through England was a triumphal procession. He received honorary degrees at Oxford, Cambridge, and Edinburgh, and was the recipient of the kindliest hospitality wherever he went, as his name had been for years a household one in England. While there, two important medical treatises were dedicated to his honor. He crossed to Paris for a week spent in visiting his old haunts and marked the many changes the political vicissitudes had brought about in that city. He called upon Pasteur in his laboratory, and speaks with the utmost appreciation of the latter's scientific labors and his great benefactions to mankind.

A year or two after his return he lost his wife, who had been his devoted companion for nearly fifty years; who had shielded him in every possible way and made his home his chief delight amid all his unusual pleasures.

His widowed daughter, Mrs. Sargent, who had come to care for him, died the year after her mother, and in 1889 he made his home in the family of his distinguished son, Mr. Justice Holmes.

Dr. Holmes felt keenly the passing away of his friends and contemporaries. He writes to one of his few remaining cronies: "The Keystone of our Arch has fallen; all we can do is to lean against each other until the last stone is left standing alone."

He did indeed live to be nearly "the last leaf upon the tree, in the spring." His physical powers were maintained with almost undiminished vigor to the end. He spent the summers at his cottage at Beverly Farm on the coast. Here he received in the most delightful kindliness many visitors who called to do reverence to the genial doctor, the sprightly autocrat, and the best talker in America. They never were disappointed. During a morning spent with the editor of the British Medical Journal who was in this country and made the usual pilgrimage to Beverly Farm, Dr. Holmes, after inquiring after many of his medical friends in England, remarked that he had passed the best years of his life as a doctor, "and I hope," he said, "they are not ashamed of me and do not reproach me for choosing to tread the flowery path of very light literature rather than chain myself for ever to the heavy tasks of medical practice." He needed to have no fears, for he, like William McClure in a very different sphere, was an honor to the profession.

And if for some I keep a nobler place;
I keep for none a happier than for thee.

—*Macaulay.*

THE BLOOD IN PERNICIOUS ANÆMIA.

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In this study of eighty-nine cases of pernicious anæmia a few features of this disease are considered from the viewpoint of the blood. We do not present any new discoveries concerning the disease, merely a few details in an as yet incomplete clinical picture.

The rule of this clinic is that at least one complete blood examination shall be made weekly in all cases of pernicious anæmia but these examinations are usually made twice weekly. We have tried to avoid deductions made from few counts, and when we speak of a "period with rising" or "falling count" we believe that we have records of sufficient blood examinations to be sure that such was the course of the blood during that period.

Several of these eighty-nine cases here mentioned were admitted more than once, hence the total number of admissions is one hundred and eight.

Primary pernicious anæmia is a disease the real causes of which are yet to be discovered, and at autopsy no lesion sufficient to explain the anæmia is to be found; hence the term "primary" anæmia. Clinically it is a very severe anæmia with signs both of blood destruction and of abnormal, or at least imperfect, regeneration. The signs of blood destruc-

tion are: the low count, the degenerations seen in the red cells, the slight jaundice, the increased urinary pigments, the occasional hæmoglobinæmia, and the increase of iron stored in the liver, spleen, and other internal organs. The evidences of abnormal regeneration are: the cells of abnormal size (macrocytes and microcytes), the distorted cells (poikilocytes), and the unusual forms of nucleated reds (megaloblasts, intermediates). There is oligochromæmia of a marked degree: the hæmoglobin runs almost parallel to the count of red cells, but the color index is usually above 1. The leucocytes are usually diminished in number, but the small mononuclear cells are always relatively, and sometimes absolutely increased. The platelets are diminished.

When studying cases of pernicious anæmia one is impressed by two features: the nonparallelism between the blood picture and the subjective symptoms, and the constant ebb and flow of the red-cell count. One sees men able to lead active business lives with only 1,000,000 red cells per cubic millimeter. Indeed, the low counts on first admissions show how severe an anæmia must be before the patients give up and consult a physician. Cases of chlorosis suffer much more when the count is about 4,000,000 cells per cubic millimeter. Again, the count seldom remains stationary, but is either rising or falling. The contrast is well seen in cases of the anæmia of myxœdema or cancer, where constancy is the rule. For the count in a given case to remain constant for any length of time is evidence against the diagnosis of pernicious anæmia. It is either rising or falling, the rate of increase and decrease sometimes being quite uniform; the periods of improvement and of relapse often succeed each other with a singular rhythm, frequently independent of subjective sensations, and almost of medication.

The Red Corpuscles.—*Count on Admission.*—The count on admission will depend on the symptom or symptoms for which the patient seeks relief. In general it is true that the first counts on these patients are the lowest of any group. To find the red-cell count under 1,500,000 in a patient who has no very evident cause for anæmia, who has not been under treatment, is almost sufficient for diagnosis.

Of our 108 first counts (of 89 patients—some had several admissions), the

lowest was 516,000
below 1,000,000, 17, or 16% of the admissions,
between 1,000,000 and 2,000,000, 56, or 52%,
" 2,000,000 " 3,000,000, 16, " 15%,
" 3,000,000 " 4,000,000, 17, " 16%,
above 4,000,000 2, " 1%,

Our cases may roughly be divided into three groups, according to the symptoms of which the patients complain: First, there are those who mention only the "shortness of breath and weakness on exertion," which seem due to the profound anæmia. These patients come in with the lowest counts. Second, there are those with gastro-intestinal symptoms; nausea, vomiting, diarrhœa, constipation, dyspepsia, etc. These symptoms begin earlier, hence these patients are admitted with counts between 1,000,000 and 2,000,000. The patients of the last group come for a varied list of ailments, but common among them are those due to a combined sclerosis which is sometimes a very early feature. Case 80 on his second admission complained of numbness in the legs, and had a count of 4,276,000, the highest first count of our series. Upon symptoms also will depend the time the patient can be persuaded to stay in the hospital, and hence the *count on discharge*. It is hard for him to accept our idea of the severity of his condition, and if he does not, he leaves when the symptoms which brought him to the clinic have disappeared. Patients of the first group who have really suffered from the weakness of the anæmia are usually willing to stay a reasonable length of time. Patients of the third group, especially those with nervous features, stay the longest; but patients of the second group, who come with gastro-intestinal symptoms, stay a short time only, since these symptoms are soon corrected, and the weakness dependent on them disappears.

Course, as judged by the red cells.—In a few rare cases the count remains quite stationary while the patient subjectively improves and soon feels so well that he insists on his discharge. Of these we cite 7 cases:

Case 70 was admitted complaining of poor digestion and general weakness, and with a red count of 1,600,000. The cells varied little and in 20 days he was discharged with 1,400,000 cells and feeling much improved. He rested a few days at home and then returned to work.

Case 69 on admission had 1,500,000 red cells. He complained of dysentery and weakness. The counts varied from 1,842,000 to 1,328,000. In 74 days he was discharged feeling much better, the count being 1,836,000.

Case 68 came in for diarrhœa and weakness with a count of 1,040,000 red cells. During 63 days the maximum count was 1,979,000 and the lowest that on admission. At the end of that time he left with a count of 1,448,000 red cells, feeling better.

Case 55 complained of indigestion, loss of weight and strength; the count was 1,368,000. During 46 days the highest count was 2,100,000, the lowest 1,368,000, and on discharge, 1,800,000. He left much improved.

Case 45 was admitted with 1,760,000 red cells and complained of "stomach trouble, pain in the liver, and weakness." During 17 days the highest count was 2,246,000, the lowest 1,700,000. He was then discharged in good condition, with a count of 1,724,000.

Case 83.—On admission the count was 1,604,000. During 109 days the red cells varied from 1,988,000 to 1,482,000, and at the end the count was 1,552,000.

Case 88.—On admission the count was 804,000. He was in the hospital 9 days. The maximum count was 1,092,000, the minimum, 804,000; at the end the count was 940,000.

These cases are interesting since they all belonged to the group mentioned above of patients who come for gastro-intestinal symptoms. They felt well enough to go home and some to work, when the count was much the same as that on admission.

Another group consisted of 24 cases whose counts rose steadily from admission till discharge. Of these, 13 left with counts between 3,000,000 and 4,000,000 and 3 with higher This represents a gain of from 40 to 260 per cent, with an average of 140 per cent, and this gain required from 30 to 120 days under treatment.

A group of 46 cases remained until the red cells had practically ceased to rise, although during the stay the counts had fluctuated considerably. In 22 of these cases the final count was between 2,800,000 and 3,800,000 red cells per cubic millimeter.

It is very difficult to get the cells to rise above 4,000,000 per cubic millimeter, and if after the cells have reached that point the patient remains in the hospital one may have the disappointment of seeing the fall of the wave. The count usually remains about 4,000,000 during the intermissions, a point of great importance in the diagnosis of the case during those periods. Two cases have recently been brought to our notice who, during intermissions, had taken as heavy life insurance as they could. Their brown pigmented, "sunburned" skin, their rather pale lips, and tinted scleræ did not attract attention. Both died within a year after their insurance examinations.

The count seldom remains constant, it usually rises or falls in regular, periodic waves. An illustration of this *periodicity* is Case 83. The cells rose for 17 days, 19,000 cells a day. They then fell for 30 days, 15,000 a day. They next rose 16,600 per day for 30 days, and then fell 13,000 per day for 32 days. The regularity of the periods and the constancy of rate of rise and fall is interesting.

Changes in the red count may be due to new formation or destruction of red cells, or to changes in the volume of the plasma. We believe the rises so often seen before death and which simulate improvement are of this latter nature.

The rate of rise and fall is interesting. During 37 periods of genuine improvement the cells rose from 30,000 to 50,000 cells per day in 16 cases, less than 30,000, in 13 cases, and over 50,000 cells per day in 8 cases. The highest was 107,000 per day. Those cases who were really "getting well" gained from 50,000 to 70,000 cells per day; we refer to the cases whose progress was clinically rapid and very satisfactory. Of 13 cases in which the rising count did not seem to mean improvement in 8 the gain was from 10,000 to 30,000, and in 4 from 30,000 to 50,000 cells per day. Of the 37 cases with genuine improvement in 10 there was a blood crisis during these periods. The gain in 6 of these 10 was from 30,000 to 66,000 cells a day. The cases with eosinophilia gained from 1000 to 80,000 cells a day. The time over which these rises extended lasted roughly from 4 to 6 weeks. Of the 16 cases mentioned above with gains of from 30,000 to 50,000 cells a day, in 14 it lasted from 4 to 9 weeks, and in one, 12 weeks. The gain of 66,000 cells a day lasted 6 weeks. Of the 13 cases with unprofitable rises, in 5 it lasted 2 weeks, and in 8 from 3 to 7 weeks.

The rate of fall was somewhat slower. Of 39 cases with periods of falling counts, in 10 the loss was from 20,000 to 30,000 cells a day, and in 25 from 10,000 to 40,000. The falls of from 20,000 to 30,000 cells per day lasted longest, from 9 to 130 days, an average of 37 days. The losses of from 1000 to 10,000 lasted on an average for 35 days. The worst loss was of 233,000 cells a day for 3 days.

Among our cases which were interesting as regards *the counts on admission and discharge*, the following groups may be cited: In one group the subjective improvement occurred during a falling count. The number of cells first rose, then fell, and the patient left when the count was about that on admission. Case 35 was admitted for "sore mouth, heartburn, and numbness and tingling of both hands." The red count was 1,908,000 per cubic millimeter. It rose for 14 days to 2,996,000 and then fell to 2,120,000, on which date he went home "well." It is interesting to note how little relation his count bore to his feelings.

More cases were admitted with a falling count, which was soon succeeded by a rising one. With the rise there was improvement in symptoms and the patient insisted on leaving when the count was practically that on admission. In Case 38 the count on admission was 2,930,000. It fell for 3 days to 2,236,000 and then rose for 8 days to 3,004,000, when he was discharged. In Case 75 the count on admission was 1,760,000. It fell for 38 days to 792,000, and then rose for 45 days to 1,624,000, at which time he was discharged. In Case 81 the count on admission was 1,756,000. It fell for 23 days to 1,373,000, and rose during the next 35 days to 1,762,000. He then was discharged.

In another group of cases the count first rose for a variable time, and the patients seemed to improve. Then it fell until death. The final count at death was sometimes almost the same as that on admission. Case 27 had on admission 767,000 cells per cubic millimeter. In 3 days it had risen to 940,000, but then began to fall, reaching in 24 days, 557,000 cells on the day of death. Case 46 had on admission 940,000 cells. At the end of 24 days the count was 1,023,000. Six days later at death it was 718,000. Case 65 is a very good illustration. This patient was admitted for "sick stomach, sick bowels, shortness of breath," and a count of 1,236,000. At the end of 63 days the count was 3,428,000. In 224 days it had fallen to 840,000, and in 18 days had risen to 1,216,000. He died the day following, and at autopsy only the lesions of a severe anæmia were found.

In some cases the count rises from the day of admission till that of death. To explain this, changes in the volume of plasma may be important. Case 78 on admission had 1,228,000 red cells. At the end of 19 days the count was 1,864,000, 8 days later it was 2,144,000, and death followed.

Another group of cases similar to this has first a falling count which then rises and continues to rise until death. Case 76 had on admission 1,192,000 cells. In 28 days it had fallen to 828,000. It then rose and in 12 days was 1,028,000. Four days later the patient died.

A recent case not included in the above series shows this

even better. The course of this patient was clinically downward during the whole period in the ward.

Date.	Reds.	Leucocytes.
July 18.....	1,550,000	4,700
" 25.....	1,815,000	7,300
Aug. 4.....	1,560,000	3,600
" 13.....	1,839,000	2,400
" 21.....	1,692,000	6,800
" 28.....	1,496,000	2,200
Sept. 11.....	1,490,000	4,000
" 25.....	1,690,000	4,800
Oct. 5.....	1,962,000	3,300
" 12.....	2,132,000	4,320
" 21.....	2,632,000	3,280
" 30.....	2,000,000	1,860
Nov. 7.....	2,860,000	1,560

The count at death is of even greater interest than that on admission. The following are all counts made within 48 hours of death:

376,000	..... the lowest,	
400,000 to 500,000	..... 3 cases,	
500,000 to 600,000	..... 3 cases,	
600,000 to 700,000	..... 4 cases,	
864,000	..... 1 case.	
Mean of above 12 cases.....		540,000.
1,000,000 to 1,100,000	..... 4 cases,	
1,100,000 to 1,200,000	..... 1 case,	
1,200,000 to 1,300,000	..... 1 case,	
1,300,000 to 1,400,000	..... 2 cases.	
Mean of above 8 cases.....		1,100,000.
2,144,000	..... 1 case,	
2,704,000	..... 1 case.	

One is tempted to divide these cases, according to the counts at death, into three sharply-defined groups, for it seems improbable that the above arrangement could be accidental. But further consideration shows that the cases are here grouped much as they were on admission. Of the first 12 cases the highest on admission was 2,048,000, the mean of all being 1,064,000, and the average of all 1,100,000; 5 were below 1,000,000. Of the 8 cases of the second group the average on admission was 1,442,000, the lowest being 1,192,000 and the highest 1,992,000. Of the 2 cases with highest counts the first counts were 1,800,000 and 2,240,000. It would seem from these few cases that the higher the count with the first symptoms, the higher it is at death.

The immediate causes of death in this disease are many. Some patients show progressive weakness and dyspnœa, are irrational, and seem to die from weakness alone. Some of these at autopsy have œdema of the lungs, but no lesions to explain death other than those of a severe anæmia. Others die of terminal infections. Eight of the 12 cases of the first group had clinically and at autopsy no cause of death, save the signs of anæmia. One died suddenly and 2 of terminal infections. Four of the second group died of terminal infections and two of "anæmia." Both of the cases of the third group died of "anæmia."

Counts on successive admissions.—While different persons come with widely different counts it often happens that the same person will come at different times with counts curiously similar, as if each person had a limit below which the red cells could not fall without symptoms severe enough to induce him to seek relief. Of course this is not always the case.

Twelve of our cases were admitted more than once; in 10 the count on second admission was lower than that on the first.

Case 68.—First count on admission was 1,060,000; on the second, 26 days later, 1,040,000.

Case 76.—On first admission the first count was 1,206,000, the last was 4,080,000. Four months later he was readmitted with a count of 1,192,000.

Case 67.—On the first admission the first count was 1,300,000, the last was 3,890,000. He was readmitted in four months' time with a count of 1,090,000.

Case 82.—On the first admission the first count was 1,928,000, the last was 2,448,000. After 13 months he returned with a count of 1,620,000, and was discharged later with the count about the same. Fourteen months later he returned with a count of 1,864,000, and was discharged with a count of 2,900,000. The fourth admission was 11 months later, and the first count was 1,638,000. At death it was 376,000.

All of the cases admitted more than once had moderately high counts at first. None were admitted with low counts.

Just as some persons are "well" when the count is about that of admission, so some die with a count which has hardly changed.

Case 9 on admission had 672,000 red cells. In ten days there was no change, and the last count was 648,000. He died two days later.

Case 19 was admitted with 516,000 cells and died four days later with 454,000.

Thirteen of our 22 fatal cases answered the description of the older writers who defined pernicious anæmia as one which progresses on a downward course relentlessly to death. A good illustration of this is the following:

Case 82 (fourth admission). We give only a few of the 42 blood examinations made.

Date.	Reds.	Hb.	Leuco.	Remarks.
Jan. 9, '04....	1,638,000	40	3000	Mononuclears 42%.
" 14, ...	1,427,000	35	3100	
" 21, ...	1,654,000	43	4100	
" 28, ...	1,515,000	35	4700	
Feb. 1, ...	1,332,000	35	3000	
" 5, ...	1,260,000	30	3600	An ineffectual blood crisis begins.
" 9, ...	1,092,000		2800	Normoblasts 896, Intermediates 4368, Megaloblasts 784 per cubic millimeter.
" 13, ...	1,064,000	27	3200	
" 16, ...	1,280,000	32	2700	Crisis at end.
" 21, ...	1,000,000	25	3500	
" 24, ...	1,064,000	27	2500	
" 27, ...	860,000	27	3200	
Mar. 2, ...	700,000	25	3400	A few nucleated reds.
" 6, ...	764,000	23	1200	Mononuclears 62%.
" 9, ...	648,000	20	1500	No nucleated reds.
" 13, ...	570,000	17	2400	
" 15, ...	376,000	13	3300	Death.

NUCLEATED RED CELLS.—A discussion of this question

should not be begun before definitions are given of the terms to be used. One reason there is such confusion concerning the occurrence of these cells is that one man calls a megaloblast a cell which others would class as an intermediate or even a normoblast. Normoblasts are, we believe, nucleated red cells, the size of the ordinary non-nucleated cells, perhaps a trifle larger, with a nucleus about 3.5 microns in diameter, round, and sharply defined. The larger nuclei have a perfect chromatin network; these cells are called "Howell's immature nucleated reds"; other cells having smaller nuclei which are very dense, stain deeply and diffusely, and which show absolutely no trace of a chromatin network, "Howell's mature cells." Between the two extremes are cells with nuclei showing every step in the process of pycnosis. All these we group as normoblasts, although many call the immature cells intermediates. By megaloblast we mean a large nucleated red with nucleus at least 7 microns in one diameter; that is, about the size of an ordinary red cell. The protoplasm may be polychromatophilic, with ragged edge, the nucleus oval, staining faintly, with a fine chromatin network of definite pattern, separated from the protoplasm by a colorless line, and with other characteristics sometimes urged as necessary to its identification but the one essential thing, we believe, is a nucleus the size of an ordinary red blood cell. Our reason for this as the criterion is the result of the study of many bone-marrows of ribs of infants, removed at operation, and at early autopsies. In all were found two types of cells with constant characteristics; the normoblasts, and cells with nuclei over 7 microns in diameter. In addition to these are cells without constant points in size, with nuclei varying from those of immature reds to those of megaloblasts. These were called intermediate nucleated reds, and may be defined as cells with bodies too large for normoblasts or nuclei too small for megaloblasts. They may perhaps have about the same significance as melagoblasts, but our rule is to call every cell concerning which there is any doubt, an intermediate. We do not count the immature cells in this group. It would seem that red cells are produced in "islands of proliferation" with megaloblasts at the center and normoblasts on the periphery, and that in perniciaus anæmia these islands are stripped of their outer zones leaving the megaloblasts to keep up the supply of red cells (Bunting).

Nucleated reds were present at some time in 62 of 74 cases; normoblasts alone in 11; normoblasts, intermediates, and megaloblasts in 45; megaloblasts and intermediates in 6. In 61 cases there were 67 periods during which nucleated cells were present for a considerable time. During 27 (44 per cent) of these periods the red cells rose; during 34 (56 per cent) they remained stationary or fell. Fourteen other periods of about equal length were chosen during which no nucleated cells at all were found, and during 8 of these red cells rose.

HÆMOGLOBIN.—The hæmoglobin is reduced to a low point, yet apparently not to quite so low a one as the count of the red cells. In our cases it was on admission, from

10 to 20%	in 19	cases,	a.
20 " 30%	" 26	"	b.
30 " 40%	" 32	"	c.
40 " 50%	" 19	"	d.
50 " 60%	" 4	"	e.
60 " 70%	" 2	"	f.
70 " 80%	" 1	"	g.

Since the reduction of hæmoglobin is not quite as great as that of red cells, the *color index* (hæmoglobin per cent divided by red cell per cent, 5,000,000 = 100 per cent) is usually greater than 1.

Index.	a	b	c	d	e	
0.6 to 1.0.....	3	9	5	1	1	total 19
1.0.....	6	4	10	5	0	" 25
1.0 " 1.5.....	6	11	15	11	3	" 46
1.5 " 1.9.....	4	2	2	2	0	" 10

The letters heading these columns are those of the preceding table, indicating the per cent of hæmoglobin. It will be seen that 81 per cent of all had at first an index over 1. The reason for this high color index, early supposed to be a characteristic feature of the disease, has been in much dispute. Among the explanations given are: that the cells are overloaded with hæmoglobin that: in this disease the hæmoglobin has a different chemical composition from the normal; there is hæmoglobinæmia; the cells are larger than normal; that hæmoglobinometers are inaccurate; the many microcytes are not counted; the average size of the cells is increased, hence there is increased volume of protoplasm to carry hæmoglobin. We have often blamed the hæmoglobinometers, especially those with a color prism. The lower half of this scale is usually rather incorrectly standardized since the prisms are planed with straight-edges and marked on the assumption that depth of color varies with thickness of the glass. The instruments with one color to standardize, as the Gowers or Sahli instruments, have especial advantages in cases with these low values. But if the error is due to the instruments, then the high indices should occur most frequently in cases with low hæmoglobin values, but a glance at the table on page 55 will show that with hæmoglobin under 30 per cent, 22 cases had an index of 1 or under, 23 over 1, while of the cases with hæmoglobin between 30 and 50 per cent, 21 had an index of 1 or less, 30 over 1.

That microcytes are overlooked in counting cells there is little doubt, and these may contain considerable hæmoglobin. One of our good workers confessed to an error of 200,000 cells in one blood count from this oversight. The evidence that the cells have pigments of an abnormal composition is, we believe, not convincing; also that there is often free hæmoglobin in the plasma which could affect the readings, we doubt. Capps, in his splendid paper, has given good evidence that the high color index is due to the increased size of the cells, not to supersaturation, and the work of Mr. Wroth in this clinic confirms this opinion.

The hæmoglobin line runs almost parallel to that of the red cells. As the case improves the index decreases; towards

death it increases. This is not always the case and sometimes the reverse is true; as for instance of 30 of our cases with improvement, in 7 the index rose, and of 17 cases with an unfavorable course, in 6 it fell. The rule, nevertheless, is that stated above, and it is not uncommon to see an index of 1.1 drop to 0.7 as the count rises, or one of 0.9 rise to even 1.7 before death. These changes may be due either to the newly-formed light-weight cells, or the increasing per cent of large cells, or to several factors.

Leucocytes.—In pernicious anæmia may occur, it is said, a leucopenia or a lymphocytosis. By leucopenia is usually understood a white count of 5000 cells or less. This was true of 74 or 75 per cent of our cases on admission. Of 99 of our admissions the first counts were as follows:

500	to 1,000	.....	2 cases,
1,000	" 3,000	.....	36 "
3,000	" 5,000	.....	36 "
5,000	" 8,000	.....	17 "
8,000	" 10,000	.....	5 "
11,000	" 20,500	.....	3 "

During the course the count varies much, in a lawless manner it would seem, but if one averages a large number of cases, the white count as a rule runs parallel to the red. As a case improves rapidly the leucocytes are high, if slowly, they often remain low. As a case nears the end and all regeneration practically ceases, the reds and whites may fall together.

		Reds.	Leucocytes.	
Case 20.—Nov.	22, '97	1,140,000	2400	
Dec.	1, '97	880,000	3000	
Dec.	4, '97	667,000	666	and death.

During their stay in the hospital 63 of our admissions showed at some time a count of 3000 cells or less. Of these, 41 improved, and 22 died. The counts were as follows:

		Cases which improved.	Which died.
500	to 1,000	1 admission	6 admissions.
1,000	" 2,000	21 admissions	8 "
2,000	" 3,000	19 "	8 "

The above counts occurred during the 63 admissions of 58 patients, of whom 20 or 34 per cent died. The mortality of all our cases with records of leucocyte counts was 32 per cent. Hence a low leucocyte count is not necessarily a bad omen.

The counts within 48 hours of death were as follows:

666	to 1,000	.....	1 case,
1,000	" 3,000	.....	4 cases,
3,000	" 5,000	.....	4 "
5,000	" 8,000	.....	4 "
8,000	" 10,000	.....	2 "
10,000	" 16,000	.....	2 "

Leucocytosis.—For the white cells to rise about 10,000 per cubic millimeter may mean one of several conditions. It may be caused by a complicating acute infection. Thus, of our cases:

Case 1, 12,000 leucocytes, had acute parotitis,
Case 9, 14,440 leucocytes, had pyelonephritis,
Case 43, 12,000 leucocytes, had pulmonary tuberculosis. (This case may also have had a blood crisis.)
Case 63, 12,800 leucocytes, died of a terminal pneumonia.
Case 39, the count of 10,400 white cells may have been due to the dysentery from which he suffered.
Case 65, with 10,300 white cells had fever and abdominal pain.

Or, the leucocytosis may be part of a blood crisis, as in Case 79, with 20,500 cells, and Case 87, with 15,600, both with a normoblastic crisis. Some patients have a terminal (agonal?) leucocytosis. Such patients are very weak, irrational, yet without fever up to the end. Case 24 had 15,200 and Case 80, 16,000 leucocytes. The autopsies did not explain the counts. In other cases no cause can be assigned, as in Case 59 with 12,000 cells. Case 69 is of considerable interest since the cells were high on both admissions, 13,000 on the first and 10,000 on the second. After both admissions the patient improved.

The Differential Count.—In pernicious anæmia especial interest rests in the differential count of the leucocytes. The small mononuclears are said to be increased both relatively and absolutely; the polymorphonuclears to be correspondingly decreased: the eosinophiles to be increased during periods of improvement; and myelocytes are said to be present in unusual numbers. The question at once arises, is there an increased formation of small mononuclears and a decreased formation of neutrophile cells, or do the latter decrease and the former seem actually increased since relatively they are so, while their absolute count remains the same?

The study of our cases convinces us that many processes exist: increased production sometimes, increased destruction (or limited production) in others, while the most important factor is the proportion of the cells, for here more clearly than in any other disease of which we know, is there a tendency for the differential count to remain the same however much the total count may change. That this is not a plasma change is seen by the red-cell counts which change independently of the number of leucocytes.

	Date.	Red cells.	Leucocytes.	Percentage of mononuclear nongranulars.
Case 64.	Oct. 26.....		3,000	28
	Dec. 10.....	2,436,000	5,125	13
	Mar. 21.....	3,508,000	3,000	34
	April 14.....	1,696,000	1,750	37
	May 2.....	1,118,000	4,000	37
	May 17.....	1,668,000	2,250	34
Case 36.	May 22.....	736,000	933	93.6
	June 15.....	513,000	6,000	93.4
Case 39.	May 5.....	1,067,000	3,200	17.3
	June 14.....	1,223,000	2,000	17.7
Case 55.	Oct. 4.....	1,795,000	3,850	40
	Oct. 12.....	1,500,000	4,000	43
	Oct. 18.....	1,800,000	4,250	39
	Nov. 6.....	1,800,000	1,800	46
Case 68.	Aug. 17.....	1,060,000	1,400	28
	Sept. 12.....	1,040,000	1,300	27
	Sept. 30.....	1,760,000	1,600	23
	Oct. 9.....	1,848,000	4,000	26

The same is true even when there is a leucocytosis.

	Date.	Red cells.	Leucocytes.	Percentage of mononuclear nongranulars.	
Case 87.	Mar. 23.....	972,000	3,840	42	
	Mar. 29.....	1,084,000	5,900	35	
	April 2.....	1,368,000	7,380	39	
	April 6.....	1,630,000	15,600	41	
	April 23.....	3,328,000	5,200	38	
Case 63.	Feb. 19.....	1,196,000	4,700	32	
	Mar. 10.....	1,280,000	4,700	32	
	Mar. 18.....		11,000	35	terminal pneumonia
Case 43.	May 3.....	1,850,000	20,500	21	
	May 9.....	1,320,000	8,000	24	
	May 15.....	1,120,000	12,000	22	
	May 22.....	1,325,000	11,500	18	
	June 6.....	1,916,000	5,250	18	
Case 24.	May 11.....	1,300,000	8,800	13	
	May 15.....	1,000,000	15,200	13	
	May 17.....	700,000	11,600	9	

All of these cases show the constancy in the differential count. In other cases the differential count seems to vary with the total count, as if one group of cells was especially involved. In some cases it resembles an inflammatory leucocytosis.

	Date.	Red cells.	Leucocytes.	Percentage of mononuclear nongranulars.
Case 9.	Sept. 30.....	672,000	4,200	26
	Oct. 7.....		14,400	13
Case 80.	Nov. 5.....	1,992,000	3,680	25
	Nov. 20.....	2,040,000	4,280	23
	Dec. 1.....	2,562,000	6,080	47
	Dec. 5.....	1,718,000	4,700	33
	Dec. 8.....	1,874,000	4,000	43
	Dec. 20.....	1,480,000	4,000	43
	Jan. 19.....	1,326,000	16,000	16
Case 69.	Oct. 15.....	1,500,000	10,000	31
	Nov. 21.....	1,328,000	3,000	20

In other cases the rise of small mononuclears is partly absolute but chiefly relative, and explained by the decrease of the granular group:

	Date.	Red cells.	Leucocytes.	Percentage of mononuclear nongranulars.
Case 74.	Feb. 16.....	1,578,000	4,800	54
	Mar. 4.....	1,202,000	2,700	38
	Mar. 30.....	1,012,000	1,250	88
	April 7.....	800,000	950	73
Case 75.	June 20.....	1,760,000	7,500	25
	June 22.....	1,616,000	3,250	37
	July 14.....	880,000	1,200	54
	July 18.....	842,000	1,500	78

LYMPHOCYTOSIS.—By this term two different conditions are understood. Some mean by it a relative increase of lymphocytes, so that they count over 25 per cent of the whole number; some an absolute increase in these cells to 2000 or more per cubic millimeter. It makes considerable difference which definition is meant, for the percentage may vary greatly while the absolute count remains unchanged if some other group of cells, especially the polymorphonuclear neutrophiles, changes considerably in absolute number. If it is true that these two groups of cells have little relationship (and this is still to be proved), then only an absolute increase can have much meaning. Since the personal element is a very strong factor in separating the small mononuclears from large mononuclears and transitionals, and since in this disease the separation of these groups is not so very important, we prefer to group them all under the heading "mononuclear nongranulars" or "basophiles" and consider 30 per cent the normal percentage and 2500 the normal absolute number.

An absolute lymphocytosis (over 2500 mononuclear nongranulars) occurred at some time during the course of 18 of 69 cases. Of these 11 died, a mortality of 61 per cent. Hence the presence of this condition seems unfavorable. It often exists just before death. These counts were, from

2500 to 3000..... 7 cases,
3000 " 3500..... 6 "
3500 " 5000..... 4 "
5580 ..... 1 case at death.

In these cases the percentages of these mononuclear nongranular cells at the time of the above absolute numbers were, from

10 to 30%..... 4 cases,
30 " 40%..... 5 "
40 " 60%..... 6 "
70 " 80%..... 2 "
93.4% ..... 1 case at death,

and the total leucocyte counts, from

4,000 to 6,000..... 4 cases,
6,000 " 10,000..... 10 "
over 10,000..... 4 "

The highest leucocyte count was 20,500, of which 21.4 per cent, or 4380, were mononuclear nongranular cells.

In case the total leucocyte count is only 3000 cells or fewer it is clear that an absolute lymphocytosis cannot exist, but it is interesting to see how many of these few cells were mononuclear nongranulars. Some time during their course 39 of our cases (with good blood records) had a total white count of 3000 or fewer. Of these the percentage of mononuclear nongranulars was in

16 cases between 30 and 40%,
10 " " 40 " 50%,

The lowest percentages were, 10.3 per cent when the total leucocyte count was 1800 cells; 16 per cent when the total leucocyte count was 1320 cells; and 17.7 per cent when the leucocyte count was 2000 cells. In 4 cases the percentages of mononuclear nongranular cells was 70 or over, and the total leucocyte counts 1500 cells or under.

A relative lymphocytosis, that is, a percentage of mononuclear nongranular cells of 30 or over, occurred in all but 6 of 69 cases. Hence there was a relative lymphocytosis in 91

per cent of our cases, an absolute in 26 per cent. Since, however, the total leucocyte counts tend to run low in this disease we must conclude that an increase in the absolute number is commonly the rule.

Eosinophilia.—The behavior of the eosinophile cells has attracted much attention since their number is believed to be an index of marrow activity. As these cells seem to bear no direct relation to other cells it is their absolute number which is important; over 250 per cubic millimeter means an increase beyond physiological limits. A percentage of over 4 usually means an eosinophilia, but not always. An increase in these cells usually accompanies a rapid increase in the red cells, but often a slow one, while towards the end their high number may be proof of energetic but unsuccessful attempts of the marrow to replenish the blood. Their increase is a common feature of a blood crisis (see page 58).

In 17 of our cases these cells rose with the red cells, and in 10 cases fell with them. The total disappearance of these cells is a bad sign.

	Date.	Reds.	Leucocytes.	Percentage of eosinophiles.
Case 24.	May 11	1,300,000	8,800	1.6%
	13	1,100,000	9,000	0
	15	1,000,000	15,200	0
	17	700,000	11,600	0
	18	637,000	9,200	death.

The disappearance of these cells may be a valuable sign in cases in which the reds are not falling.

	Date.	Reds.	Leucocytes.	Percentage of eosinophiles.
Case 60.	July 22	2,832,000	5,200	
	23	2,769,000	3,400	5.4%
	27	2,568,000		
	30	2,888,000	4,500	4.0%
	Aug. 3	2,672,000	5,500	
	6	2,704,000	4,000	
	7	death.		

A true eosinophilia occurred in 11 cases, 3 of whom died. The count of the eosinophile cells was:

250	to 300	2	cases,
300	" 400	3	"
400	" 500	4	"
630	" 858	4	"

while these cells were of the total leucocyte count, from

3	to 4.0%	1	case,
4	" 5.0%	2	cases,
6.3	" 9.2%	6	"
14.7	and 15.6%	2	"

In 5 cases the red cells were rising, while the eosinophile count was high; in 5 they were not rising; in one case the point was not determined. In 3 cases the eosinophile count was highest on admission.

The behavior of these cells in a case during improvement is well illustrated by the following:

	Date.	Reds.	Leucocytes.	Eosinophile per cent.	Eosinophile count.
Case 51.	Oct. 8	1,892,000	4,250		
	9		3,500	2.4	84
	11	1,921,000	2,500	5.4	135
	21	1,788,000	3,700		
	31	2,000,000	2,500		
	Nov. 4	1,608,000	2,000		
	14	1,800,000	1,600		
	22	2,860,000	1,200		
	Dec. 5	2,850,000	5,000	7.5	375
	7	3,424,000	3,800	5.5	210
	12	3,600,000	5,300	3.3	175
	19	3,508,000	5,100	3.7	190
	26	3,624,000	5,000	7.6	380
	Jan. 1	3,600,000	6,500	4.0	260
	9	3,952,000	7,500	5.0	375
	15	3,804,000	6,700	3.7	350
	23	3,532,000	6,000	3.3	198
	30	3,604,000	5,000	3.3	165
	Feb. 6	2,600,000	4,150	5.0	208
	19	2,500,000	3,600	7.1	256
	20	2,900,000	2,800	6.2	173
	27	3,000,000	2,400	7.0	168
	Mar. 6	3,100,000	2,100	14.75	315
	13	3,740,000	3,700	9.8	349
	20	3,848,000	3,700	6.3	233
	27	3,872,000	6,200	6.8	422
	April 3	3,820,000	6,000	4.3	258
	11	4,208,000	8,000	3.8	304
	17	4,302,000	6,500	2.3	150

A *relative eosinophilia* (over 4 per cent), the above cases not included, occurred in 15 cases. Four of these died. Of these 15 cases, in 3 the reds were rising at the time the percentage of eosinophiles was high, in 6 they were not rising, in 5 they were falling, and in one it was doubtful. These percentages were from

4	to 5%	4	cases,
5	" 6%	4	"
6	" 7%	3	"
7	" 8%	2	"
9	" 10%	2	"

and the total leucocyte counts were

	1,000	1	case,
1,000	to 2,000	5	cases,
2,000	" 3,000	4	"
3,000	" 4,000	4	"
5,000		1	"

While a rise of the eosinophile cells may mean increased marrow activity, it certainly does not always mean that the prognosis is good.

Myelocytes occur more constantly and in greater numbers in pernicious anæmia than in any other disease except leukæmia. In 28 of our cases they were present in numbers varying from 0.2 to 0.8 per cent ,and in the majority of these from 0.4 to 0.8 per cent.

Blood Crises.—A blood crisis may be defined as a period during which large numbers of nucleated reds are present in the peripheral blood. v. Noorden thought that they occurred while the bone-marrow was especially active in the formation

of red cells, and that they were followed by a jump in the red-cell count. The leucocytes, especially the eosinophiles, should also rise. While in cases of chlorosis and of secondary anæmia blood crises may be evidence of improvement, in pernicious anæmia this is by no means always the case. The most strenuous attempts of the exhausted bone-marrow to stem the tide of blood destruction may be fruitless, and the remarkable display of nucleated reds and leucocytes in the blood may be described as analogous to the muscular convulsions preceding death.

An arbitrary line must of course be drawn to define a blood crisis. That which seemed most natural, judged by our cases, was 50 or more nucleated reds per 1000 leucocytes. Accepting this number as a limit, blood crises occurred in 14 of 70 cases.

There are two kinds of blood crises, and seldom is there doubt in this classification: the normoblastic and the megaloblastic. They are classified according to the predominating nucleated red cell. Intermediate cells are here counted as megaloblasts. By normoblastic crisis is meant a period during which there are present in the circulating blood 50 or over nucleated reds per 1000 leucocytes, and the majority of which nucleated reds are normoblasts. This occurred in 5 of our cases. The nucleated cells varied:

normoblasts	.....from	192	to	5896	per 1000	leucocytes,
intermediates	..... "	0	"	112	" 1000	"
megaloblasts	..... "	0	"	161	" 1000	"

Four of these accompanied a rising red count. In the fifth the reds remained constant.

	Date.	Reds.	Leucocytes.	Normoblasts per cubic millimeter.
Case 10.	April 18....	1,792,000	11,750	5,896
	May 5....	2,720,000	20,500	

			(Per 100 leucocytes.)				
	Date.	Red.	Normoblasts.	Intermediates.	Megaloblasts.	Leucocytes.	Eosinophile per cent.
Case 10.	Mar. 29...	1,084,000	16	14	12	5,900	2.6%
	April 2...	1,368,000	106	62	101	7,280	3.0%
	6...	1,630,000	1064	112	8	15,600	5.5%
	16...	2,887,000	0	0	2	5,320	8.5%
	23...	3,328,000	0	2	0	5,200	14.0%
	May 3...	3,672,000					

This is a complete crisis, with the many nucleated reds, the leucocytosis, the eosinophilia, and the good result.

There were 9 megaloblastic crises. The cells varied as follows:

normoblasts	.....	10	to 1400	
intermediates	.....	0	" 460	
megaloblasts	.....	36	" 240	per 1000 leucocytes.

During 7 of these there was a fall in the red count, in 2 a slight gain. The difference in the efficiency of normoblastic and megaloblastic crises is very evident.

The leucocytes during these crises numbered from

1,000	to 2,000	.....	3 cases,
2,000	" 3,000	.....	4 "
3,000	" 7,000	.....	5 "
11,750	and 15,600	.....	2 "

Even the greatest crisis may not be efficient. In Case 80 the crisis continued 19 weeks. The reds first rose from 1,902,000 to 2,562,000, and then fell to 1,328,000 at death. The leucocytes varied from 3000 to 5000 till death when the count was 16,000. The normoblasts were always above 500 per 1000 leucocytes. On one day there were 14,388 normoblasts, 460 intermediates, 138 megaloblasts, and 239 microblasts per cubic millimeter. This was shortly before death while the total red count was falling.

A NOTE ON THE VOLUME AND COLOR INDEX OF THE RED CORPUSCLES.

By PEREGRINE WROTH, JR., M. D.

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In an article, entitled "A Study of Volume Index," published in "The Journal of Medical Research" for December, 1903, Dr. Joseph A. Capps, of Rush Medical College, described the relation existing between the hæmoglobin content and the cubic contents of red cells in various diseases. His exhaustive study of 175 cases, including all kinds of anæmias, in all stages of progress, leaves nothing new to be said, but at the suggestion of Dr. Emerson 11 cases of anæmia which have been in our wards this spring have been studied in the same manner in which Dr. Capps studied his cases.

The points made by Dr. Capps which come out most clearly in the following cases are these:

(1) In primary anæmias the cell volume is increased.

(2) In secondary anæmias the cell volume is decreased.

(3) Red cells do not become supersaturated with Hb., that is the increase in Hb. content never exceeds the increase in cell volume; but on the other hand in secondary anæmias the decrease in Hb. content may be more marked than the diminution in the size of the cell.

In the cases studied the following method was used:

(1) The number of red cells per cubic millimeter was determined in the usual way.

(2) The Hb. percentage was determined in the first 6 cases by the Sahli hæmometer and the reading corrected so as to correspond to the standard Miescher in use here. In the last 5 cases the Miescher instrument was used directly, 14 g. of Hb. per 100 cc. being taken as 100 per cent.

(3) The volume of the cells was determined by the hæma-

tocrit, fresh blood, unaluted by any fixing fluid, being used, and the machine rotated for at least four minutes, 50.3° on the scale, Daland's latest figures, being taken as the reading for 5,000,000 normal cells.

(4) The diameter of the individual cell represents the average of 150 measurements made with an eye-piece micrometer which had been standardized before using. The cells were measured in the fresh state. No crenated cells or cells showing shapes not approximately normal were included.

(5) The thickness of the cell and the cubic contents of the individual cell were calculated from the reading on the hæmatocrit, the number of red cells, and the average diameter. These figures thus are not actual measurements, but merely percentages, the normal thickness being considered 1.00, and the normal cubic contents 1.00.

(6) The color index is the quotient obtained by dividing the Hb. per cent by the percentage of red cells per cubic millimeter, 5,000,000 red cells of course being 100 per cent.

(7) The volume index, a term proposed by Capps, is "the percentage volume of red cells (determined by the hæmatocrit) divided by the percentage number of cells. This will give the percentage volume of the individual cell.

(8) The surface, as I have called it here, is not the surface of the red cell in square microns, but merely the percentage surface, the surface of the normal cell being considered 1.00.

In Cases I, II, and III, the hæmatocrit was not used.

Case	No. of reds.	Hb.	C. I.	V. I.	Hæmat.	Diam.	Surface.	Thick.	Cu. Cont.		
I.	4,836,000	87	.9	....	....	7.31μ	.94	....	....		
II.	2,358,000	69	1.46	....	....	8.85μ	1.39	....	....		
III.	1,644,000	49	1.5	....	....	8.69μ	1.34	....	....		
IV.	1,756,000	16	.45	.56	10	6.7 μ	.79	.7	.56	G. per 100 cc.	New C. I.
V.	4,424,000	71	.806	.85	38	7.76μ	1.07	.8	.85		
VI.	3,840,000	33.5	.44	.48	18.8	6.9 μ	.84	.58	48		
VII.	4,636,000	55.4	.59	.73	34.5	6.81μ	.82	.9	.73	7.76	.64
VIII.	4,072,000	69.5	.85	.804	32.9	7.68μ	1.02	.789	.804	9.73	.92
IX.	3,820,000	39.2	.51	.59	23.7	7.08μ	.89	.66	.587	5.49	.54
X.	2,552,000	59.8	1.10	1.12	29.07	9.08μ	1.46	.77	1.12	8.37	1.27
XI.	800,000	16	1.00	1.04	8.4	8.6 μ	1.31	.79	1.04	2.25	1.07

CASE I.—Practically normal. Cell a trifle small, C. I. correspondingly decreased.

CASES II AND III.—Cases of pernicious anæmia. The C. I. is high, that is, the Hb. content of the cell is greater than normal, but at the same time with the increased diameter as shown by measurement the surface is increased to almost as great an extent as the Hb. content.

CASE X.—Also a case of primary anæmia. (In this and the following cases the hæmatocrit was used.)

The following points are clear:

(1) The cell diameter is increased considerably more than Hb. content.

(2) The cell thickness is decreased.

(3) Volume index is greater than color index, that is the cell has increased more in size than it has in Hb. content. In other words, though the Hb. content is increased the cell is not supersaturated with Hb.

CASE XI.—Clinically a case of pernicious anæmia, though the color index is just 1.00. In this case with Hb. content at normal, the size of the cell has increased. This might be taken as confirming Capps' statement that the volume index is a more trustworthy guide than the color index, as to whether we are dealing with a primary or secondary anæmia.

CASES V AND VIII.—These are secondary anæmias.

The following points are made out:

(1) Low color index.

(2) Cell diameter greater than normal.

(3) But thickness of cell has decreased to such an extent that

(4) Cubic contents (volume index) is less than normal, and corresponds very closely to the value expressed by the low color index.

Here then are two cases of secondary anæmia, in which with a low color index, we have a cell which as seen under the microscope appears larger than normal, the decrease in volume being due to the great decrease in thickness.

In CASES IV, VI, AND IX, the anæmia is of the secondary type, and the cell is decreased both in diameter and thickness. The decrease in volume as shown by the volume index is practically the same as the decrease in Hb. content as shown by the color index.

CASE XI is a case of secondary anæmia which bears out Capps' statement that the decrease in Hb. content often exceeds the decrease in volume, that is, the cell lacks considerably being saturated with Hb.

In only one case in the series is there a suggestion of supersaturation with Hb., Case VIII, one of the secondary anæmias.

As said before, in Cases VII to XI inclusive, the Hb. was calculated in grammes per 100 cc. and it is therefore possible to compare the new color index proposed by Dr. Emerson with the volume index as determined by the hæmatocrit.

This new color index is determined by dividing, in any given case, the "grammes per million" by the factor 2.63, this factor being the normal "grammes per million." By referring to the table it will be seen that in every case the new color index is higher than the old color index, and in three cases (VII, X, and XI) is considerably higher than the volume index. This difference is due to the fact that in the first calculations 14 g. of Hb. per 100 cc. was taken as the normal, while in the determination of the new color index 13.15 g. of Hb. per 100 cc., a quantity which Dr. Emerson has found to be more nearly correct for the normal person, has been taken for 100 per cent.

Judged simply by these few cases it would seem that a cell can be supersaturated with Hb., but of course it will require a great number of observations on the relation between the volume index and the new color index before anything definite can be said.

PULSATING EMPYEMA.

By W. J. CALVERT, *Columbia, Mo.*

In this second paper on pulsating empyema,[1] I wish to reconsider some factors of the subject in the light of some experimental work recently done by myself in Dr. C. W. Green's Physiological Laboratory.

Experiment.—A cannula connected with a mercury manometer was inserted in the right carotid artery. A cannula connected with a mercury manometer and a large bottle of normal salt solution was inserted in the pericardium. From the bottle, salt solution was allowed to flow into the pericardium under varying pressures and the intra-pericardial pressures and pericardial pulsations were recorded along with the pulse.

This experiment demonstrated that, when the pericardium is distended with fluid, there is a pericardial pulsation with each heart cycle. The tracings show that as the pulse curve rises the pericardial curve falls. When the pulse curve is highest the pericardial curve is lowest and as the pulse curve falls the pericardial curve rises. The pulsation of the pericardium which is diastolic in time is caused by the diminution in the size of the heart during systole and directly to the blood leaving the heart. As a portion of the blood leaving the left ventricle passes out of the thorax to the head and arms, the amount of blood passing through the thoracic aorta is less than the contents of the left ventricle. (The blood in the right ventricle remaining within the thorax may be disregarded.) The end result is that the thoracic contents are diminished in systole by the heart's contraction and increased by the distension of the aorta. The distension of the aorta in systole cannot compensate for the diminution in the size of the heart because a portion of the blood passes immediately out of the thorax to the head and arms and out of the thoracic into the abdominal aorta. (The amount of blood flowing into the thorax through the large veins in this short interval of time is of very little practical importance in this consideration.)

The thoracic cavity becomes smaller during systole by the amount of blood which leaves the cavity. If under normal conditions a pulsation occurs it should be diastolic in time, as is true of the pericardium, and for the same reasons.

In pleurisy and empyema the factors necessary to produce a pulsation of the thoracic wall are as follows: a firmly fixed pulsating organ; contact of the pleural wall with this pulsating organ; distension of the pleural sac with fluid, air, or solid material, and collapsed condition of the lung. The first requirement is fulfilled by the thoracic aorta; the second, by the normal relationship of pleural wall to thoracic aorta; the third, by presence of fluid, pus, or a combination of these with air in the pleural cavity; and the fourth, by the collapsed condition of the lung in pleurisy and empyema. With each increment of pressure the weakest portion of the wall will expand first.

As a direct factor in causing the pulsation the heart may be excluded or else the pulsation must be diastolic in time. The sudden flow of blood into the aorta causes the vessel to suddenly become larger or to pulsate.

The intra-pleural pressure must be sufficiently great to stretch the pleural wall to a degree which will permit them to take up the systolic diminution in the size of the thorax and remain sufficiently taut to respond to the sudden increase in size of the thoracic aorta, or to manifest a systolic pulsation synchronous with the pulsation of the aorta. When the weakest portion of the pleural wall is external that portion must pulsate.

The right ventricle forces a certain amount of blood into the compressed lung which must be larger during systole and consequently add a minor factor to the intra-pleural pressure and consequently to the systolic pulsation.

The anatomical relationship of the aorta to the right and left pleura has been previously described and accounts for the frequency of left-sided pulsating pleurisy and empyema.

Dr. Sailer[2] has reviewed in detail the literature, to 1904, on pulsations of the thoracic walls and their causes.

[1] W. J. Calvert, "The Cause of Pulsation in Empyema." The Am. J. Med. Sciences, Nov., 1905, p. 890.

[2] Joseph Sailer, "A Study of Circumscribed and Diffuse Pulsation of the Wall of the Thorax." The American Journal of Medical Sciences, August, 1904.

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LETTER FROM CAMPBELL P. HOWARD, M. D.

BERLIN, NOVEMBER 21, 1906.

To the Editor of The Johns Hopkins Hospital Bulletin, Baltimore, Md., U. S. A.

DEAR SIR:—Professors Welch, of Baltimore, and Blackader, of Montreal, suggested that a letter to your journal concerning "the Medical Advantages of Munich," might prove of interest to your readers. First as to Munich itself. There is scarcely any city in Europe, that has so many attractions for a visitor as Munich, situated as it is in the beautiful valley of the Isar, within sight of the snow-capped Bavarian Alps and easy access of endless excursions. Art flourishes in Munich, as evidenced by the picture galleries, which contain some of the most celebrated paintings in Europe, and by the music, which is excellent—the opera being second only to that of Wien. The rate of living is moderate, the pensions numerous and for the most part comfortable, the people polite, sympathetic and (to use a favorite expression of their own)—*gemütlich*. Lastly, for one who has yet to learn the language, Munich has exceptional advantages, because the English-speaking people are not so numerous that one cannot escape them (a statement which cannot be made of Berlin or Wien); hence one can, if one so desires, associate with a German-speaking "Kreis." Yet one is in a city of nearly 600,000 people, with good theaters, concerts, art galleries, and other diversions for the home-sick "Ausländer."

As to medicine. The "Königliche Ludwig-Maximilians Universität" has a medical faculty of which it has a just right to feel proud, and one that lives up to the high standards set by its former teachers—Pettenkofer, Ziemsen, etc. It includes at present such men as Voit, in physiology; Rückert, in anatomy; Bollinger and Dürck, in pathology; Gruber, in hygiene; Angerer, in general surgery; Lange, in orthopedics; Winckel, in gynæcology and obstetrics; Bauer, Müller, and May, in medicine; and Kraepelin, in psychiatry. For the "course-crazed" student Munich offers no facilities when compared with Berlin or Wien, but one can occupy his day very well with a schedule, which would include the majority of the above-mentioned teachers.

It is especially to those interested in internal medicine that Munich is to be highly recommended. For one who has just graduated from the medical school, but above all for one who, having served two or three years as an "Interne" in a general hospital, wishes to specialize in internal medicine, Munich is the place "par excellence." In the morning he can hear lectures on morbid anatomy by Bollinger and Dürck, attend the theater clinic of Friederich Müller, work in the poliklinik with May, and in the afternoon study psychiatry with Kraepelin.

A man, who has a moderately good training and speaks and writes German, may procure a "Volontärship" in the wards of Professor Müller, the value of which can only be realized by a visit to the two hundred and fifty public beds, which comprise the service of the "second klinik." If one does not write and speak German sufficiently fluently or does not wish to do "clinical routine," one can obtain work in the laboratory, where, under the guidance of Professor Müller and his assistants, an original "Arbeit" in chemistry, bacteriology, or pathological histology may be undertaken. Professor Müller has surrounded himself with an unusually capable group of assistants, each of whom is a specialist in some experimental line of work, and, therefore, best fitted to investigate certain series of cases. Naturally the room in the laboratory is limited, and a man desiring such work must satisfy Professor Müller as to his qualifications and undertake to stay a definite length of time (three to six months).

A word as to Müller as a teacher. He ranks among the first three men in clinical medicine in Germany and is considered by many the best teacher. His lectures are simple, thorough, and painstaking. His cases are carefully prepared and honestly presented, and a student, no matter how advanced, never leaves his lecture-room without having acquired some new fact or thought, even though the text be a time-worn one, as typhoid or pneumonia. He is an inspiring teacher, a practical physician, and a scientist in the best sense of the term. His great interest in the chemical side of medicine is especially stimulating, and his lectures on the diseases of metabolism are most instructive. By the teacher of clinical medicine his methods of teaching are well worth careful consideration and imitation, and a visit of a week or two in his klinik will never be regretted.

Hoping that this letter will prove of assistance to some of your readers, who, wishing to spend "a year abroad," are undecided as to the choice of the klinik, and thanking you for so much of your valuable space. Believe me,

Yours truly,

CAMPBELL P. HOWARD.

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STUDIES IN GENITO-URINARY SURGERY

THE JOHNS HOPKINS HOSPITAL REPORTS, Volumes XIII and XIV, will be issued in January, 1907. Volume XIII will consist of about 605 pages with 201 figures in the text, six plates and one colored chart.

Volume XIV will consist of about 632 pages, and have 97 figures in the text.

The price of each volume will be five dollars ($5.00), bound in paper, and five dollars and fifty cents ($5.50), bound in cloth.

Remittances and orders will now be received.

THE JOHNS HOPKINS PRESS, BALTIMORE, MD.

NOTES ON NEW BOOKS.

The Physicians' Visiting List. (*Philadelphia: P. Blakiston's Son & Co., 1907.*)

This small pocket note-book is a useful one for any doctor; it is well arranged, beginning with a calendar for 1907-1908; it contains tables of incompatibility, of antidotes and doses, etc.; followed by a visiting list with special memoranda for 25 patients per week. In all senses it is handy and helpful.

Review of the Practice of Gynecology. By DR. J. W. BOVEE. (Lea Brothers & Co., Philadelphia and New York, 1906.)

It may be true that Gynecology as a specialty is "passing," but the number of new books each year and new editions of older works devoted to this branch of surgery indicates that it still has no small degree of vitality. A recent addition to the literature is the Practice of Gynecology, edited by Dr. J. W. Bovee. This work is a collaboration by American authors. It is intended chiefly for the general practitioner, and omits, therefore, much of interest to the specialist. It includes chapters on diseases of all of the pelvic organs, as well as the ureters and kidneys in the female, thus treating more than formerly belonged to the province of the gynecologist.

The book as a whole is well written, well illustrated, clear and complete. It has some of the faults which are difficult to avoid in a collaboration. The arrangement of the chapters is not logical, urinary fistula coming early, after displacements of the uterus, and diseases of the rectum and anus being introduced between diseases of the vagina and inflammations of the uterus. There is some repetition. Two pictures of Fowler's position are unnecessary, as are also two detailed descriptions of vaginal hysterectomy, with plates. Prolapse of the uterus scarcely receives the attention it deserves.

There are numerous excellent chapters, of which those on examinations, inflammations of the uterus, fibro-myomata of the uterus, infections of the tubes and ovaries, and extra-uterine pregnancy, are especially good.

In regard to radical operation for malignant disease of the uterus, the writer takes a wise middle position suitable for a text-book. The author of the vaginal method of operating, while presenting the subject well, writes as an advocate and does not give impartial views. The chapter on post-operative treatment and complications of abdominal operations dismisses renal complications as "of frequent occurrence. Indeed the function of no organ demands more careful and constant attention after operation than the kidney." Three lines are, however, adequate. Cystitis is better. It receives six lines (see page 530).

The index is good and the press work of the usual high standard of the publishers.

Progressive Medicine. Vol. III. September, 1906. Section on Obstetrics. (*Philadelphia and New York: Lea Brothers & Co., 1906.*)

This review of the year's work in Obstetrics covers one hundred pages and is based on seventy-five papers of which eleven are from the French and the Italian, while the remainder are about equally divided between German and English publications (including American). Among the periodicals of this country the clippings from the New York Medical Journal have a noticeable predominance.

The literature on "The Toxæmia of Pregnancy" is exclusively represented by massive quotations from two papers. One of these "On the Chemistry of Toxæmias of Pregnancy" is purely theoretical and has for its chief purpose the undermining of a suggestion by Williams that the ammonia coefficient of the urine may be taken as a guide in differentiating the grave cases of vomiting of pregnancy. The method has been in practical use in the obstetrical clinic of the Johns Hopkins Hospital for three years and remains the most reliable means we possess for determining where an abortion is necessary and where it is not. Wolf's quoted opinion that the ammonia variation in these cases depends on the patient's weight is not in accord with the facts and consequently his deductions are valueless.

The only other contribution of the year to toxæmia which the reviewer regards worthy of mention is Edgar's "Clinical Manifestations." In this a futile effort is made to classify toxæmias according to symptoms. Clearly, no logical classification is possible save that in which the pathological lesions are taken as criteria. It naturally follows that Edgar's papers add confusion to the subject of toxæmia of pregnancy and represent a backward rather than a progressive trend.

Undue space and prominence is often given to ludicrous therapeutic suggestions. Two pages are occupied with the report of a case of eclampsia in which recovery has followed the use of copious enemata of milk sugar. Again, a detailed account of Koplinski's view of the value of pork in treating the vomiting of pregnancy is quoted. This style of diet is recommended, because it is so heavy "that ejection from the stomach is wellnigh impossible."

The section on "Obstetric Surgery" is the most satisfactory portion of the review. The citations here give a fair idea of the contention which exists regarding the relative merits of vaginal Cæsarean section and dilatation of the cervix with the instrument of Bossi, though it is not made clear to the reader that the weight of authority and experience is in favor of the cutting operation.

Pubiotomy is duly credited with a steady increase in popularity. The gain in length of the various diameters of the pelvis, the anatomical relations of the site of operation, and the prevailing technique in its execution are discussed in the light of recent contributions.

The section on "The Puerperal Period" relates almost altogether to the bacteriology of the uterus after delivery in normal as well as in infected cases. A continued lack of agreement is shown with regard to many practical points, such as, the advisability of the antepartum douche, the possibility of auto-infection, and the proper therapeutic measures when infection has occurred. The review points no distinct advance in these problems during the past year and is characterised by an indecisiveness that we feel is unfortunate. The practitioner is left in grave doubt where sound wisdom could be supplied, if the reviewer would give more space to monographs founded on careful and conscientious work, eliminating ridiculous papers and such as lack the ear-marks of honest laboratory experiment or clear-minded clinical observations.

J. MORRIS SLEMONS.

The Nervous System of Vertebrates. By J. B. JOHNSTON, PH. D., Professor of Zoology in West Virginia University. Pp. I-XX + 370, with 180 illustrations. Price $3. (*Philadelphia: P. Blakiston's Son & Co., 1906.*)

This book will be read with much eagerness by those who feel dissatisfied with the customary cumbersome method of presenting the comparative anatomy of the nervous system. It is an outgrowth of previous papers by the same author, and consists of a description of the vertebrate nervous system based on its functional analysis. Under the influence of Gaskell he divides the brain and cord into four primary longitudinal systems, and uses them as units of description. The success which he has had in demonstrating the fundamental character of these units indicates the possibility of the introduction of such a basis of analysis into general use.

There are those who may not agree with him in some of his interpretations; as for instance, where (p. 328), he attributes the degeneration of the forward end of the hippocampus in higher vertebrates to the growth of the corpus callosum; others might say that the rudimentary hippocampus was the result of a rudimentary olfactory end-organ, and that the presence of the corpus callosum was an unrelated coincidence. Also some will disagree with him where (p. 176) he classifies the olfactory apparatus under the visceral sensory system, instead of placing it, like the optic apparatus, under the modified cutaneous or somatic sensory system. Under the neurone theory he omits the cell-chain hypothesis of fiber formation, and what is more important makes no mention of Harrison's experiments on the histogenesis of nerve fibers. All through the text there is scant reference made to authorities. This is to be regretted inasmuch as the author is apparently thoroughly familiar with the literature and it would have been of great convenience to the reader. Such things of course are only details, the real thing to be considered is the fact that the author has given us a new presentation of the whole vertebrate nervous system which not only portrays its essential morphology, but does this in terms of function, consistent with a living mechanism.

G. L. S.

A Practical Treatise on Fractures and Dislocations. By LEWIS A. STIMSON, B. A., M. D., LL.D., Professor of Surgery in Cornell University Medical School, etc. Fourth edition. Revised and enlarged. (*New York and Philadelphia: Lea Brothers & Co., 1905.*)

The fact that this work has passed through four editions testifies to its popularity and worth.

Since the last edition, the very general use of the X-ray and the frequent use of the open operation have contributed a great deal to our knowledge of fractures, especially those into and near the joints. In the revision of his book, the author has made full use of the knowledge thus acquired. The chapters dealing with fractures and dislocations of the carpal bones and fractures of the lower end of the humerus in children have been largely rewritten.

A large number of skiagrams have been added, which increase the value and attractiveness of the volume.

Essentials of Human Physiology. By D. NOËL PATON, M. D., etc. Second edition, revised and enlarged. (*Chicago: W. T. Keener & Co., 1905.*)

According to the preface the object of this work is to put into the hands of medical students a volume emphasizing those parts of physiology which are of special interest and importance to the future practitioner. In the execution of this worthy intention the author has not been markedly successful.

It is to be regretted that no distinction should have been drawn between systolic and diastolic blood pressures and that the author should have confined himself to the bold assertion that the Hill-Bernard instrument may be used for the determination of the blood-pressure in man (p. 258). The truth of many of the author's statements might be called into question as for instance where it is affirmed that the absence of the pulse in the veins is due to the low resistance offered to the passage of the blood toward the heart (p. 247), or where one reads that the vagus is "a true excito-motor nerve of the respiratory center" and is stimulated only during collapse of the lungs (p. 293).

Sometimes an incomplete account is as bad as one which is frankly incorrect as for instance the treatment of venous pulsations (p. 255), and of sleep (p. 177). Now the reader is tempted to ask how the contracting heart pulls upon the lungs in order to produce the cardio-pneumatic movements (p. 297), and again to wonder at the remark that there is no evidence in favor of the neurogenic hypothesis of cardiac contraction (p. 238).

If a text-book cannot be original it may at least be well written, accurate and, as far as it goes, complete. It is unfortunate that the work in question has none of these qualities.

PERCY M. DAWSON.

An Introduction to Physiology. By WILLIAM TOWNSEND PORTER, M. D., Associate Professor of Physiology in the Harvard Medical School. (*Philadelphia and London: J. B. Lippincott Company, 1906.*)

Those who are concerned with the science of education cannot afford to be ignorant of the opinions of Professor Porter. According to Professor Porter physiology should be taught in the laboratory by means of experiments performed by the student himself. These experiments should not be performed for the purpose of clearing up notions gained from books and lectures, but on the contrary they should be regarded as of primary importance and serve as the point of departure for such reading as may be necessary for their explanation and correlation. The method of Professor Porter may be of questionable value in handling large classes, but if so it is possible that all other methods which really teach anything are open to the same objection.

The Introduction to Physiology is an excellent expression of the author's views. It is therefore not an ordinary laboratory manual. Its aim is not only to give directions for a long series of feasible and important practical exercises, but to explain and discuss (sometimes with references to the original literature) the methods and apparatus employed and the results obtained. The seventy-four illustrations are simple in character, but clear and well chosen. It is to be regretted that there are no chapters on mammalian vivisection, a branch of physiology of the greatest importance to medical students. This is, however, the fault not of the author but of the antivivisectionists who, with the best intentions, are limiting the efficiency of medical education in some sections of the country.

Those who are of Professor Porter's way of thinking will see in the introduction an epoch-making work; while those who do not agree with him will nevertheless find it an extensive, very helpful and well written laboratory guide.

PERCY M. DAWSON.

The Thirteenth Annual Report of the Craig Colony for Epileptics. By DR. WILLIAM P. SPRATLING. Sonyea, N. Y.

The Thirteenth Annual Report of the Craig Colony for Epileptics just issued contains 106 pages. It is profusely illustrated in a way to show all sides of colony life.

The Colony embraces 1695 acres of land, comprises at present 76 houses, with six more going up for 200 additional patients. The present census is nearly 1300 all told; when the new buildings are completed the total census will be approximately 1500. There are now about 1000 epileptics in the State who cannot be received, because there is no room.

A new departure in Dr. Spratling's report this year is a special section devoted to scientific papers and reports made up of articles contributed by members of the medical staff. That the amount of surgical work alone performed at Sonyea is considerable, is shown by the fact that anæsthetics for surgical purposes were given 172 times during the year.

A modern hydrotherapeutic plant after the plans of Dr. Baruch has been installed and the plant has been a valuable feature in the treatment of certain types of epilepsy.

The net per capita cost of keeping each patient at the Colony last year was $141.38. We believe this is about $35 a year less than keeping an insane person in a State Hospital for the insane.

There is a movement on foot initiated at the Colony to establish a second Colony for epileptics nearer New York City.

The Johns Hopkins Hospital Bulletins are issued monthly. They are printed by the LORD BALTIMORE PRESS, Baltimore. Single copies may be procured from NUNN & CO., and the BALTIMORE NEWS CO., Baltimore. Subscriptions, $2.00 a year, may be addressed to the publishers, THE JOHNS HOPKINS PRESS, BALTIMORE; single copies will be sent by mail for twenty-five cents each.